THE THERMAL CONDUCTIVITY OF ORGANIC VAPOURS : THE INFLUENCE OF MOLECULAR INTERACTION

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Summary

A study has been made of the thermal conductivities of a number of simple organic vapours at various pressures and temperatures. The measurements indicate that the variation of conductivity with pressure is a function of gas imperfection ; for substances with appreciable dipole interaction the effect is large, but for other substances where gas imperfection involves only van der Waals forces, the effect is much less. In all cases it is probable that the change in specific heat of the vapour with pressure is the main cause of the observed conductivity variation.

I. Introduction

According to kinetic theory the thermal conductivity of an ideal gas should be independent of pressure. Experiments on real gases have shown this to be substantially correct for permanent gases such as argon or air, and the slight conductivity variations sometimes detected with change in pressure of these gases have generally been attributed to faulty apparatus design or experimental technique. The behaviour of imperfect gases in this respect has not yet been investigated fully, and the object of the present work was to study the pressure dependence of the thermal conductivity of various organic vapours for which the gas imperfections are large.

Similar measurements with organic vapours have been carried out previously by Lambert, Staines, and Woods (1950). They observed two separate effects : (i) strongly polar compounds exhibited a large linear increase in thermal conductivity with increasing pressure ; this effect diminished markedly with increasing temperature and was attributed to molecular association of the vapours ; (ii) non-polar compounds showed a relatively small linear increase in thermal conductivity with increasing pressure, and this became larger as the temperature was raised.

In the present measurements the second observation has not been confirmed. For non-polar compounds the results indicate a smaller dependence of the conductivity on pressure than that reported by Lambert *et al.*, and furthermore the effect distinctly *decreases* as the temperature is raised. The results for polar compounds agree well with the earlier measurements.

II. Experimental

(*a*) *Apparatus*

The instrument used was of the hot-wire type, and is illustrated diagrammatically in Figure 1. The design was similar to that described by Lambert

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et al., but to decrease convection and accommodation effects, the conductivity tubes were narrower and the conductivity wires thicker than those of the earlier apparatus. In addition special care was taken in mounting the wires, to reduce extraneous thermal gradients in the system.

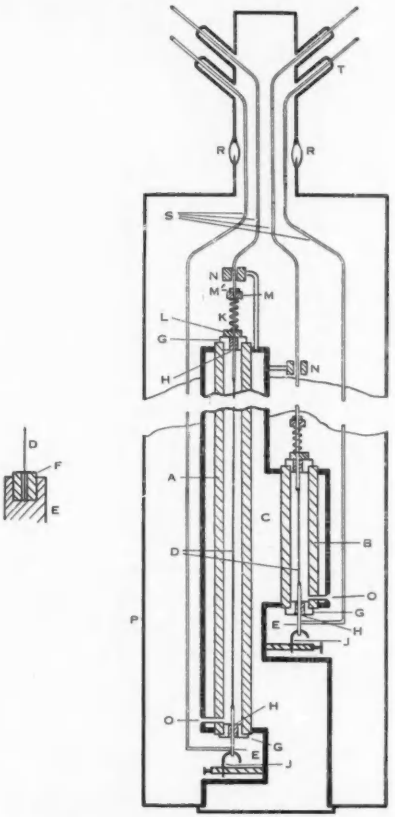

Fig. 1.—Thermal conductivity apparatus.

The conductivity tube *A* (length 25 cm.) and the smaller tube *B* (length 6 cm.), which compensates for " end effects " in the main tube, were of drawn brass, $\frac{1}{4}$ in. external diameter. They were silver-soldered into carefully bored $\frac{1}{4}$ in. holes in a solid brass rod *C* (diameter 1 in.), and an oversize reamer (diameter 2·5 mm.) was passed down each tube to ensure that the bore was uniform and straight.

Fine platinum wires *D* (diameter 1/10 mm.) were stretched along the axis of each tube being supported at their ends by thicker platinum wires *E* (diameter

1 mm.). To make certain that the fine wires were mounted centrally in these end pieces, accurately made platinum sleeves *F*, holding the wires, were fitted into small holes in the end pieces (see insert) and then the wires were silver-soldered under slight tension. Brass collars *G*, lined with thin insulating glass sleeves *H*, were pushed tightly into the ends of each tube, and through these the well-fitting thicker platinum end wires *E* were introduced. This arrangement ensured that the fine wires *D* were situated exactly at the axis of each tube.

At the lower ends of the tubes the wires *E* were fixed to small glass hooks *J*, which insulated them from the body of the apparatus ; at the upper ends weak platinum springs *K*, resting on thin insulating glass disks *L* were used to provide slight tension in the wires *D*, and small nuts *M* (with lock nuts *M'*) regulated the compression of the springs. The wires *E* were finally passed through glass locating plugs *N* fixed to the body of the apparatus. Since during conductivity measurements there must be easy access of vapour to the platinum wires within the conductivity and compensating tubes, three small holes *O* (diameter 2 mm.) were drilled at the bottom of each tube to provide a vapour passage.

The whole assembly was contained in a wide brass tube *P* soft-soldered at the base ; it was connected by a metal-glass seal *R* to the vacuum system and vapour supply. Flexible, multiple-strand copper leads *S* were silver-soldered to the ends of the conductivity wires, and tungsten-glass seals *T* provided external connections to the electrical system. The completed conductivity cell was mounted vertically in a thermostat, controlled by means of a sensitive mercury/glycerine regulator with a "Sunvic" proportioning head ; during experiments the temperature remained constant to at least one-hundredth of a degree ($\pm 0{\cdot}005$ °C.). Temperature measurements were made with a calibrated thermometer graduated in 0·1 °C., and minor variations in temperature were noted on a Beckmann thermometer. Glycerine was used as thermostat liquid above 65 °C., and water at the lower temperatures.

The apparatus was evacuated by means of a mercury diffusion pump with an efficient liquid air trap. Glass sections of the apparatus were wound with nichrome wire and kept at approximately 20 °C. above the temperature of the thermostat liquid. Taps were greased with silicone grease.

The pressures of the compounds used were measured with a sylphon bellows heated sufficiently to prevent condensation. As the pressure of the vapour in the apparatus was varied, a small steel cylinder attached to the bellows moved in or out of two coils of wire, and the corresponding change in the mutual inductance of the coils was registered on a sensitive meter. This gauge proved effective at pressures above 10 cm. Hg, when pressure readings accurate to within about $\pm 0{\cdot}3$ cm. could be made. Calibration of the gauge was carried out using a mercury manometer as standard, and with air in the apparatus. The calibration was repeated before each series of measurements.

Vapour was admitted to the evacuated system from a small bulb of liquid. The liquid was warmed and a tap opened until the required pressure of vapour was set up in the apparatus.

The electrical circuit was identical with that used by Lambert, Staines, and Woods (loc. cit. ; cf. also Mann and Dickins 1932). The conductivity wire

and compensating wire were connected in opposite arms of a Callendar and Griffiths bridge on which the resistance of the apparatus was measured. By means of a sensitive potentiometer the current flowing in the wires was determined from the potential drop across a standard ohm coil placed in series with the wire in the compensating tube.

(*b*) *Experimental Procedure*

With an apparatus of the present type the thermal conductivity of a vapour is compared with that of air at the same temperature. The experimental procedure was similar to that described by Lambert *et al.* Air, dried and freed from carbon dioxide, was introduced into the apparatus, and the current required to maintain the wire in the conductivity cell at a temperature about 7 °C. above that of the thermostat was measured. Readings were taken at different pressures and the square of the current $I^2_{(p)\,\mathrm{air}}$ was plotted against the corresponding pressure. At room temperature the graph was linear down to less than 30 cm. Hg (see Fig. 2), but down to pressures of only about 40 cm. at 110 °C. Extrapolation to zero pressure gave $I^2_{0\,\mathrm{air}}$.

The apparatus was then pumped out and vapour introduced. Similar measurements were made with the vapour, and again a (linear) graph of the square of the current $I^2_{(p)\,\mathrm{vap.}}$ against pressure was plotted. This was extrapolated to zero pressure and $I^2_{0\,\mathrm{vap.}}$ obtained. From the equations

$$K^\circ_{\mathrm{vap.}} = \frac{I^2_{0\,\mathrm{vap.}}}{I^2_{0\,\mathrm{air}}} \cdot K^\circ_{\mathrm{air}},$$

and

$$K_{\mathrm{vap.}} = \frac{I^2_{(p)\,\mathrm{vap.}}}{I^2_{0\,\mathrm{vap.}}} \cdot K^\circ_{\mathrm{vap.}},$$

the conductivity of the vapour at zero pressure and pressure p was calculated. Values for the absolute conductivity of air at the various temperatures were obtained from the results of Kannuluik and Carman (1951) whose recent measurements cover the range −183 to 218 °C.

Since the heat transfer from the wire to the wall of the conductivity tube depends upon the temperature difference between them, the temperatures of both must be held constant while measurements are made. The wall temperature was assumed to be that of the thermostat. The temperature of the wire was determined by calibrating it as a platinum thermometer in the following manner: air at about 60 cm. pressure was introduced and with a suitable current I flowing through the wire its resistance R was measured. Using several values of I and R a linear graph of I^2R against R was plotted from which, on extrapolation to $I^2R=0$, the resistance of the wire at the temperature of the thermostat was obtained. This procedure was repeated at all thermostat temperatures; the measurements fitted a platinum thermometry equation of standard form and from this equation the temperature of the wire was calculated.

For conductivity measurements at a particular thermostat temperature the Callendar and Griffiths bridge was set so that the wire temperature was

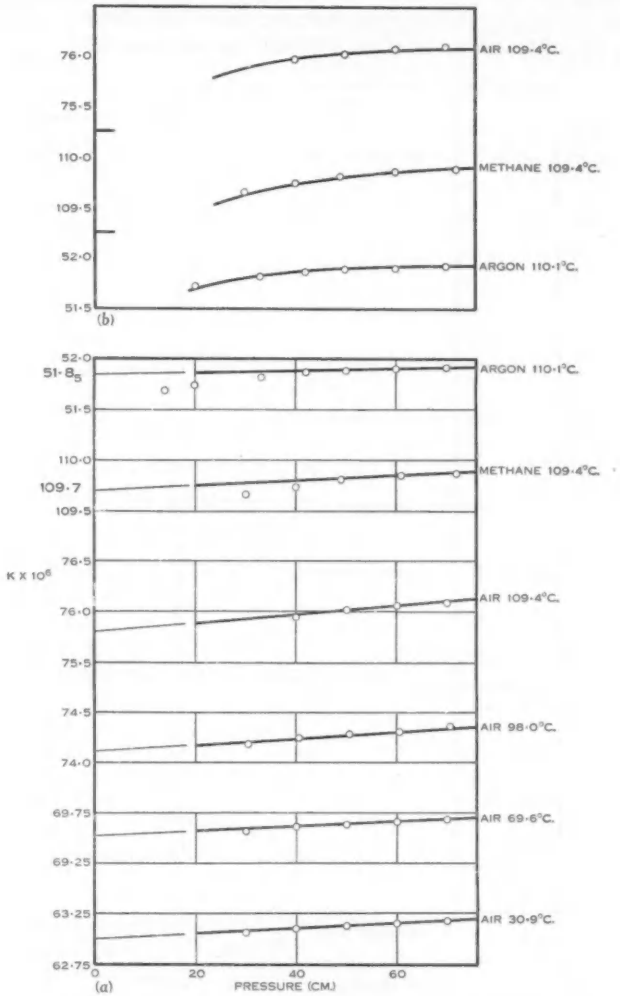

Fig. 2.—The variation in the conductivities of air, argon, and methane with pressure. In (*b*) the curves represent the influence of incomplete accommodation.

higher by about 7 °C. This setting was maintained permanently throughout all subsequent measurements. The current was varied with a series of rheostats

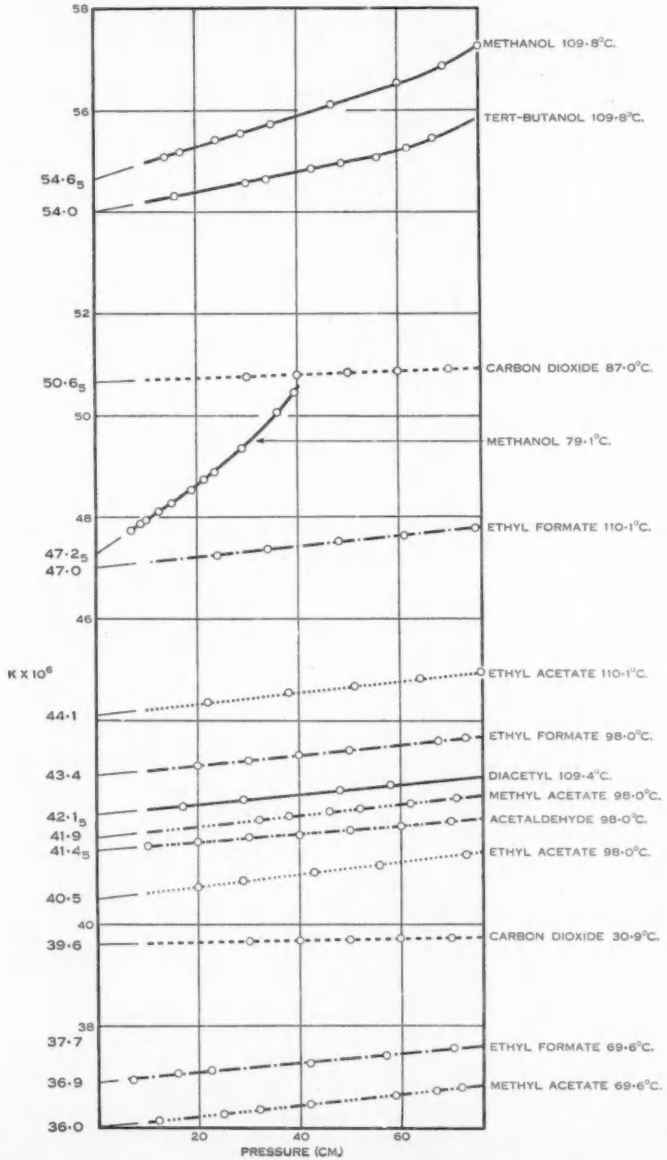

Fig. 5.—The variation in the thermal conductivities of organic vapours with pressure.

for some minutes after the pump had been shut off; under these conditions contamination of the next vapour introduced was negligible, and reproducible results could be obtained.

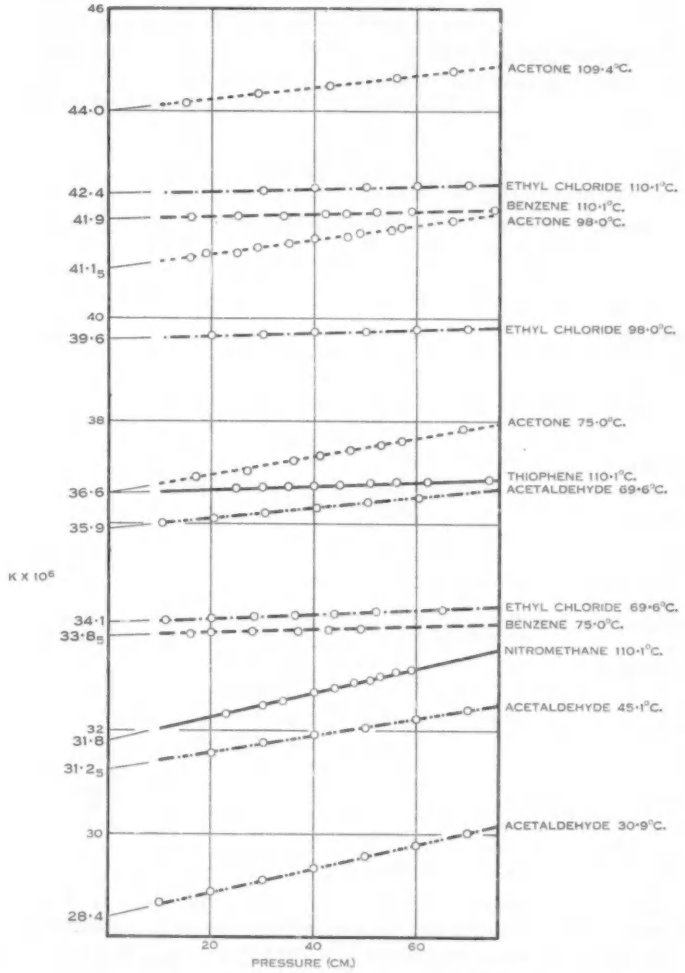

Fig. 6.—The variation in the thermal conductivities of organic vapours with pressure.

(c) *Experimental Accuracy*

During each experiment the wire temperature remained unchanged and the thermostat temperature was usually constant to within 1/500 °C.; the relative conductivity measurements on a single vapour are thus accurate to about

1 in 3000. It is difficult to estimate the error in the absolute measurements, but it is unlikely that the accuracy is better than 1 in 300.

III. Results

(*a*) *The Variation of Conductivity with Pressure.* β *Values*

The variation in the thermal conductivities of the various vapours with change in pressure is shown in Figures 2, 3, 4, 5, and 6. It may be seen that there is a linear increase in conductivity with increasing pressure for all

Table 1

β values of organic compounds (% atm.$^{-1}$)

Temperature (°C.)	30·9	45·1	55·6	69·6	75·0	79·1	87·0	98·0	100·7	109·4	109·8	110·1
Air	0·3			0·3				$0·3_5$		0·4		
Carbon dioxide	0·4		0·4				0·5					
Nitromethane												$5·5_5$
Methanol						10·9					4·3	
tert.-Butanol											$2·7_5$	
Acetaldehyde	6·5	$4·0_5$		$2·1_5$				$1·4_5$				
Diacetyl										1·8		
Acetone					(3·6$_5$)*			$2·6_5$		2·0		
Ethyl acetate								$2·2_5$				$2·0_5$
Methyl acetate				2·3				2·0				
Ethyl formate				(2·0)				$1·8_5$				$1·7_5$
Methylene bromide												1·7
Ethylidene chloride				(1·7$_5$)				1·2		1·1		
Ethylene dichloride										$0·7_5$		
Ethyl chloride				$0·8_5$				$0·5_5$				0·5
Chloroform					(1·4)			$1·2_5$		0·8$_5$		
Diethylamine				1·1				1·0		$0·9_5$		
Triethylamine								(0·6$_5$)		0·7		
Ether					1·2							$0·9_5$
Thiophene												0·8
Benzene					0·6							$0·4_5$
Hexane					$0·4_5$						$0·3_5$	$0·3_5$
*cyclo*Hexane						0·5†			$0·3_5$†			
Methane										(0·1$_5$)		
Argon												(0·1)

* Values in parentheses are uncertain.

† Values obtained on a new apparatus.

compounds except methanol and *tert.*-butanol; in these two cases the increase is at first linear but becomes greater at higher pressures. The linear increase may be represented by the equation

$$K = K^{\circ}[1 + (\beta/100)p],$$

where K is the conductivity at pressure p (in atm.) and K° is the conductivity at zero pressure. β, defined as the percentage increase in the thermal conductivity over a pressure range of one atmosphere, is a measure of the slope of the conductivity curve and has a characteristic value for each vapour.

The β values obtained from the present measurements are shown in Table 1. It is clear that polar vapours have a greater variation of conductivity with pressure than non-polar vapours. For example, the strongly polar alcohols and nitromethane exhibit the largest β values ; ether and chloroform which are less polar have β values a good deal smaller, and the non-polar substances such as benzene, hexane, and *cyclo*hexane have β values which are smaller still, though certainly greater than zero. The relatively large variation of conductivity with pressure observed for polar compounds has been attributed to molecular association (Schäfer and Foz Gazulla, 1942 ; Foz Gazulla, Colomina, and Garcia 1948 ; Lambert, Staines, and Woods 1950). However, as will be shown later, the effect could also be due to dipole interaction.

The β values of organic compounds decrease as the temperature is raised. This may be seen from Table 1 where the same behaviour is exhibited by both polar and non-polar substances. For air and carbon dioxide β appears to show a slight increase with increasing temperature. However, this effect is instrumental and is due to incomplete molecular accommodation in the apparatus (see Section IV).

(*b*) *Comparison with Previous Work*

If the β values in Table 1 are compared with previous measurements of other workers, there is good correlation between the results for polar compounds both as regards the magnitude of β, and its variation with temperature. This is exemplified by the results for methanol in Table 1A. Similar correlation is obtained for acetone, acetaldehyde, and ethyl chloride.

TABLE 1A

β VALUES FOR METHANOL (% ATM.$^{-1}$)

Temperature (°C.)	β	Observer
65·9	18·0	Lambert, Staines, and Woods
79·1	10·9	Present work
79·3	*c.* 10·5	Foz Gazulla, Colomina, and Garcia
85·0	8·0	Lambert *et al.*
100·1	*c.* 6·0	Foz Gazulla *et al.*
109·8	4·3	Present work

On the other hand, for the non-polar vapours benzene, hexane, and *cyclo*hexane (and also for ether and chloroform) the measurements of Lambert *et al.* indicate that β increases with temperature. No such effect is observed in the present results ; moreover, for these compounds the values of β reported here are roughly half the earlier values. The discrepancies are greater at higher temperatures and for vapours of large specific heat. Since convection would be expected to increase with temperature and to depend upon the specific heats of the vapours introduced, it follows that convection could be responsible for

the differences observed. Lambert and Scrivins (personal communication) recently obtained measurements more in line with the present results.

(c) *The Variation of Conductivity with Temperature*

The curves in Figures 3–6 have been extrapolated to zero pressure. The conductivity values so obtained at different temperatures are shown in Figure 7, in which the previous results of Lambert *et al.* are also included for comparison.* Over the relatively small temperature range involved in these experiments an

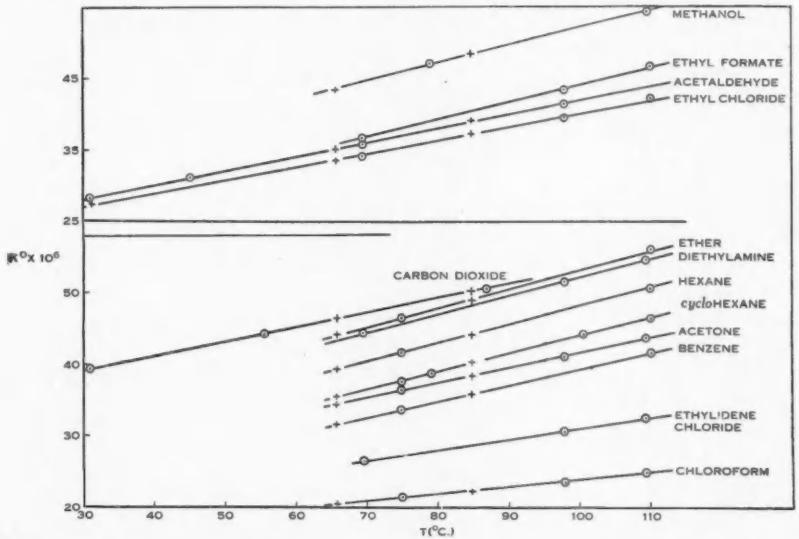

Fig. 7.—The variation in the thermal conductivities of organic vapours with temperature.
+ Results of Lambert *et al.* ⊙ Present results.

almost linear increase of thermal conductivity with temperature may be assumed, and with this in mind it is seen that there is good agreement between the two sets of results.

Using the equation

$$K^\circ_{(T\,^\circ\mathrm{C.})} = K^\circ_{(0\,^\circ\mathrm{C.})}[1+\alpha T],$$

the thermal conductivities of the vapours at 0 °C. and the mean temperature coefficients α in the range 0–100 °C. have been calculated from the slopes of the lines in Figure 7. The values obtained are only approximate; they are given in Table 2 and, for reasons which will become clear later, the corresponding specific heats of the vapours have also been included.

* These earlier results have been recalculated using Kannuluik and Carman's values for the conductivity of air. All results have been corrected as far as possible for accommodation effects (see Appendix II).

TABLE 2

THERMAL CONDUCTIVITIES AND SPECIFIC HEATS* OF ORGANIC VAPOURS

Vapour	Temperature Coefficient of Thermal Conductivity (α)	C_v at 50 °C. (cal. mol.$^{-1}$)	Conductivity at 0 °C. $K°_{(0\,°C.)}$ (cal. cm.$^{-1}$ sec.$^{-1}$ deg.$^{-1}$)
*cyclo*Hexane	$1{\cdot}38\times10^{-2}$	c. 27	$18{\cdot}5\times10^{-6}$
Benzene	1·35	c. 20	16·7
Ethyl formate	1·32	c. 27	19·0
Hexane	1·17	c. 34	22·1
Diethylamine	1·01	—	25·9
Ether	0·95	c. 27	27·1
Acetone	0·92	c. 17	21·5
Ethylidene chloride	0·89	—	16·4
Acetaldehyde	0·89	c. 12	22·1
Ethyl chloride	0·88	c. 13	21·3
Methanol	0·88	c. 9	27·8
Chloroform	0·67	c. 14	14·3
Carbon dioxide	0·60	c. 7	33·2

* Specific heats from Landolt-Börnstein; see also Lambert and Rowlinson (1950).

IV. DISCUSSION

The results for the variation of conductivity with pressure will be discussed under three headings : permanent gases, non-polar vapours, and polar vapours. In the case of permanent gases it will be shown that the variation is due to instrumental effects. For the organic vapours the β values are real, and variation in the conductivities of the vapours with pressure is closely related to the variation of their specific heats with pressure.

(*a*) *Permanent Gases : Accommodation Effects*

In the design of an apparatus to measure thermal conductivities, particular care must be taken to minimize the effects of incomplete molecular accommodation, and to reduce temperature discontinuities at the walls. If this is done, the variation in thermal conductivity of an inert gas with change in pressure is found to be extremely small at pressures up to a few atmospheres. For example, Kannuluik and Donald (1950) using a concentric cylinder apparatus could not detect any change in the conductivity of argon at 0 °C. over a pressure range of 1 atm., and in an extension of these experiments the same result was obtained even at a temperature of 300 °C. (Kannuluik and Carman 1952). In the present measurements the value of β for argon, although small, is still appreciable (0·1 at 110 °C.). It is thus possible that the observed value is the result of accommodation effects in the apparatus ; this view is supported by the fact that the " fall off " in the conductivity of the gas is perceptible at a pressure as high as 50 cm. (see Fig. 2).

The behaviour of argon in this respect suggests that accommodation effects might likewise be involved in the β values obtained for air. This idea was put forward and recently confirmed by Lambert and Scrivins (personal communication). In a series of very careful measurements at lower pressures they determined the accommodation coefficient of air in their thermal conductivity apparatus, and from the results they calculated the effect of incomplete accommodation on the conductivity results at higher pressures. It was shown that their "apparent" β values for air could be ascribed almost entirely to accommodation effects.

At a given temperature the conductivity K of a gas at pressure p is given by

$$K=K_\infty \Big/ \left(1+\frac{AK_\infty}{p}\right),$$

where A is a constant and K_∞ is the conductivity of the gas independent of pressure effects.* Assuming an accommodation coefficient for air of *c.* 0·7 at 110 °C. (Lambert and Scrivins obtained the value 0·74 for air at 66 °C.), the equation becomes $K \simeq K_\infty/[1+(0\cdot13/p)]$, where p is measured in cm. Hg.

The corresponding "variation" of conductivity with pressure is shown in Figure 2 (*b*) where comparison is made with experimental values. It may be seen that the method of Lambert and Scrivins accounts well for the observed variation; if one assumes that change in the specific heat of air with pressure makes a further small contribution towards the change in conductivity with pressure, the experimental β value is completely accounted for.

In Figure 2 (*b*) curves showing the effect of incomplete accommodation in the measurements on argon and methane at 110 °C. are also included. For both argon and methane the value of AK_∞ is approximately 0·14, corresponding to a value for the accommodation coefficient of argon of *c.* 0·75 (Thomas and Olmer 1943) and for methane of *c.* 0·6 (Grilly, Taylor, and Johnston 1946). In each case the apparent variation of conductivity with pressure is satisfactorily explained.

Accommodation effects are also important for carbon dioxide. Assuming an accommodation coefficient of *c.* 0·6 at 87 °C. (Grilly, Taylor, and Johnston 1946), the value of AK_∞ is approximately 0·10. This does not account completely for the observed β value of 0·5, but the discrepancy is explained if the variation of specific heat with pressure is also taken into account—see following section.

* If r_1 is the radius of the conductivity wire and r_2 the radius of the conductivity tube, it can be shown further that AK_∞ is related to the "temperature jump distance" g, by the expression $AK_\infty r_1 \cdot \log r_2/r_1 = gp$. The product gp is itself given by

$$gp=\frac{2-a}{a}\cdot\frac{(2\pi MRT)^{\frac{1}{2}}K_\infty}{(\gamma+1)C_v},$$

(see Kennard 1938, p. 314), where M is the molecular weight of the gas in the apparatus, a the accommodation coefficient, and γ is the ratio C_p/C_v. From these equations the value of AK_∞ may be obtained if the accommodation coefficient is known.

(*b*) *Non-Polar Vapours*

For organic vapours the accommodation coefficients are close to unity, because of the ready occurrence of adsorption, and the effects of incomplete accommodation are therefore small except at low pressures. This conclusion is verified by the linear character of the conductivity curves in Figures 3, 4, 5, and 6.

It is clear that some further explanation must be found for the pressure dependence of the conductivity of vapours, and in this connection it is of interest to determine the change in the specific heats C_v of the vapours with pressure. This is given by

$$C_v = C_{v_0} - \left[\frac{2dB}{dT} + \frac{Td^2B}{dT^2}\right]p, \quad \ldots\ldots\ldots\ldots\ldots\ldots (1)$$

where p is the pressure and B the second virial coefficient (see, for example, Roberts 1933, p. 120). dB/dT and d^2B/dT^2 may be obtained by differentiating the expression derived from the Berthelot equation

$$B = \frac{9RT_c}{128p_c}\left[1 - \frac{6T_c^2}{T^2}\right],$$

p_c and T_c representing the critical pressure and temperature.

On substitution in (1) it is found that the increase in C_v over a pressure range of 1 atm. is $1{\cdot}7\ T_c^3/p_cT^3$.* If it is assumed that the percentage increase in conductivity over 1 atm. is equal to the corresponding percentage increase in specific heat, the following expression for β is obtained:

$$\beta = \frac{1{\cdot}7\ T_c^3}{p_cT^3C_{v0}} \cdot 100.$$

Values of β have been calculated from this expression, using critical constants obtained from Landolt-Börnstein (1923–36) and specific heats from the sources listed by Lambert and Rowlinson (1950). In Table 3 the β values so calculated are compared with the experimental values. For strongly polar vapours such as methanol the Berthelot equation is unsatisfactory and no agreement can be expected. For polar compounds such as ether and chloroform the agreement is better, although the discrepancies are still considerable, but in the case of weakly polar and non-polar compounds for which the Berthelot equation is valid, there is good correlation. It is clear that for non-polar vapours, variation of specific heat with pressure accounts well for the pressure dependence of conductivity.

In Table 3, β values are also calculated for air, carbon dioxide, methane, and argon. At the temperature of the experiments these substances are above their critical points, and since the Berthelot equation no longer applies at

* Since the Berthelot equation holds only approximately, differentiation could lead to anomalous values for d^2B/dT^2, and to a smaller degree for dB/dT. As the term containing d^2B/dT^2 is significant in equation (1), considerable error might be possible in this substitution. Investigation shows, however, that over the limited temperature range involved in the present measurements the Berthelot equation is a very good approximation (see Appendix I). Thus for non-polar vapours β values calculated from equation (1) should be sufficiently accurate for comparison with experiment.

temperatures much beyond the critical temperature the values shown may be inaccurate. Nevertheless, the errors will be small since the values in question are not large.

TABLE 3

COMPARISON OF OBSERVED β VALUES WITH THOSE CALCULATED USING THE BERTHELOT EQUATION

Vapour	Temperature (°C.)	$\beta_{calc.}$	$\beta_{obs.}$	Remarks
Methanol	66	0·8	18·0	Polar compounds: No correlation between observed and calculated β values, although agreement is closer for the more weakly polar substances
	110	0·5	4·3	
Ethyl acetate ..	98	$0·4_5$	$2·2_5$	
	110	0·4	2·0	
Ether	75	0·4	1·2	
	110	$0·2_5$	$0·9_5$	
Chloroform	75	$0·7_5$	1·4	
	110	$0·5_5$	$0·8_5$	
Ethylene dichloride	110	0·5	$0·7_5$	
Ethyl chloride ..	70	$0·5_5$	$0·8_5$	
	110	$0·3_5$	0·5	
Triethylamine* ..	110	$0·7_5$	0·7	Compounds in which molecular interaction is small. Good agreement between observed and calculated β values
Thiophene*	110	0·7	0·8	
Benzene	75	0·7	0·6	
	110	0·5	$0·4_5$	
Hexane	75	$0·4_5$	$0·4_5$	
	110	$0·3_5$	$0·3_5$	
*cyclo*Hexane	79	$0·5_5$	0·5	
	101	0·4	$0·3_5$	
Air	31	0·1	0·3	Accommodation effects are sufficient to account almost entirely for observed β values
	110	$0·0_5$	0·4	
Carbon dioxide ..	87	0·2	0·5	
Methane	110	$0·0_5$	$0·1_5$	
Argon	110	$0·0_2$	0·1	

* The specific heats of triethylamine and thiophene are unknown, and the results are calculated on the assumption that C_{v_0} for both these vapours is about 20 cal./mole.

(*c*) *Polar Vapours*

It is interesting to attempt a calculation for polar vapours similar to that described in the previous section. If the second virial coefficient B is known as a function of temperature T, then β can be calculated from equation (**1**). The work of Lambert *et al.* (1949) has shown that by assuming a reversible dimerization in certain polar vapours, the experimental values of the second virial coefficients may be satisfactorily explained; in particular they have shown that $B_0 = B - RT/K_p$, where B_0 is the observed virial coefficient, B the value given by the Berthelot equation, and K_p is the equilibrium constant of the dissociation

process. Dimerization thus makes a contribution $B_{(d)}$ to the second virial coefficient where

$$B_{(d)}=\frac{-RT}{K_p}=\frac{-1}{K_c}=\text{const. } e^{\Delta U/RT},$$

ΔU being the heat of association at constant volume.

This division of the second virial coefficient into two parts cannot strictly be justified on theoretical grounds; thus calculations based on this concept may be somewhat ambiguous. However, in the present context, such a procedure is useful and is probably better than attempting to fit an arbitrary equation involving temperature to experimental values of the second virial coefficient. Differentiation of the above expression and substitution in equation (1) gives

$$C_v=C_{v_0}+\frac{(\Delta U)^2}{RT^2K_p}\cdot p.$$

From this equation it is clear that

$$\beta_{(d)}=100(\Delta U)^2/RT^2K_pC_{v_0}, \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (2)$$

where $\beta_{(d)}$, the β value attributable to dimerization, is related to the experimental β value by the expression

$$\beta_{(d)}=\beta_{\text{expt.}}-\beta_{\text{Berthelot}}.$$

Values of β derived from equation (2) are shown in Table 4: the small correction $\beta_{\text{Berthelot}}$ $(=170\ T_c^3/p_cT^3C_{v_0})$, which strictly should be subtracted from

TABLE 4

COMPARISON OF OBSERVED β VALUES FOR POLAR VAPOURS WITH β VALUES CALCULATED ON THE ASSUMPTION OF VAPOUR ASSOCIATION

Vapour	T (°C.)	ΔU* (cal. mol.$^{-1}$)	C_{v_0}† (cal. mol.$^{-1}$)	K_p‡ (atm.)	$\beta_{\text{calc.}}$ / 2·5	$\beta_{\text{obs.}}$
Acetaldehyde ..	31	c. 3600	c. 11·2$_5$	40	6·4	6·5
	45		c. 11·7$_5$	56	4·0	4·0$_5$
	70		c. 12·5	92	2·0	2·1$_5$
Methanol	66	c. 5600	c. 9·2$_5$	38	16	18**
	79		c. 9·5	51	10·8	10·9
	110		c. 9·7$_5$	c. 100	4·5	4·3
Acetone	75	c. 4800	c. 18·5	55	3·8	3·6$_5$
	98		c. 19	80	2·3	2·6$_5$
	109		c. 19·5	c. 120	1·4	2·0

* Values of ΔU have been obtained from Table 5, in which values of ΔH, the heat of association at constant pressure, are given.

† Specific heats from sources listed by Lambert and Rowlinson (1950).

‡ Values of K_p are taken from the results of Lambert *et al.* (1949); for methanol and acetone the K_p measurements may be misleading, since association to higher polymers is considered possible (cf. Weltner and Pitzer 1951).

** Result of Lambert, Staines, and Woods (1950).

the experimental values before comparison is made, has been omitted. The calculated values are, in all cases, approximately 2·5 times larger than the experimental values; possible reasons for this discrepancy will be discussed in the next section.

In the derivation of equation (2) the assumption of molecular association is not strictly necessary. Most types of molecular attraction (for example, dipole interaction) involve an approximately exponential dependence of the second virial coefficient on temperature and thus lead to an expression for β of similar form to equation (2). Nevertheless, the assumption of association provides the simplest means of evaluating β, and may be justified in certain cases. With the alcohols, for example, it is probably better to describe the type of interaction involved as association by hydrogen bonding rather than as extensive dipole interaction,* although fundamentally such a distinction is somewhat arbitrary. However, for substances such as chloroform or ether dipole interaction is the more likely cause of the discrepancies between the calculated and observed β values in Table 3.

The Treatment of Schäfer and Foz Gazulla.—An expression very similar to equation (2) has also been derived by Schäfer and Foz Gazulla (1942). On the assumption that an equation for the thermal conductivity of a perfect gas may be applied to a vapour mixture containing double and single molecules, they obtain

$$\beta_{(d)}=\frac{100}{K_p}\left[\frac{0\cdot412\Delta H\Delta U}{RT^2C_{v_0}}-0\cdot388\right]. \quad \ldots\ldots\ldots \quad (3)$$

Over the temperature range of the present experiments, assuming reasonable values of ΔU and C_{v_0} and remembering that $\Delta H=\Delta U+RT$, equation (3) reduces to

$$\beta_{(d)}\simeq41\cdot2(\Delta U)^2/RT^2K_pC_{v_0}. \quad \ldots\ldots\ldots\ldots \quad (4)$$

Comparing equations (4) and (2) it is clear that the factor 41·2 in place of the factor 100 entails excellent agreement between β values calculated from (4) and those determined experimentally (cf. Table 4). It would thus appear that, for polar vapours, the theoretical treatment of Schäfer and Foz Gazulla is preferable to that put forward in the present paper.

The derivation of Schäfer and Foz Gazulla requires that variation of pressure has *two* effects on the thermal conductivity of an associating vapour: firstly, a purely thermal effect resulting from molecular association and involving the heat of dimerization—this is represented by equation (2); and secondly, an interrelated transport effect which takes into account the differences between the molecular diameters and mean free paths of associated molecules and those of single molecules. This second effect is responsible for the factor 0·412 in

* It may be noted that methanol has a greater β value at 110 °C. than *tert.*-butanol. This observation is confirmed by the work of Foz Gazulla, Garcia-Banda, and Perez-Masia (1951), who suggest that "molecular association in the alcohols is diminished as the number of radicals around the –OH group is increased."

equation (3). It has been suggested that the first effect may equally well be connected with dipole interaction as with molecular association; but in the absence of any satisfactory theoretical treatment of the transport properties of polar vapours, the second effect is to be correlated only with an actual association process. The success of the theory of Schäfer and Foz Gazulla thus points to the conclusion that in polar vapours molecular association really does take place, with the formation of stable dimers capable of surviving a large number of molecular collisions, in contrast to mere transient complexes resulting from dipole attraction.

However, it is not yet possible to reach any unambiguous decision on this question. The equations used by Schäfer and Foz Gazulla in deriving equation (3) are not strictly applicable to real gases, and until a more rigorous theory of the transport properties of polar gases has been proposed any conclusion as to the molecular complexity of the vapours is uncertain. The present results show that the variation in thermal conductivity of polar vapours with pressure is directly related to the corresponding variation in specific heats, but the magnitude of the factor relating them cannot be established with certainty on theoretical grounds.

The Variation of β *with Temperature.*—From the standpoint of the association theory discussed above, equations (2) and (4) provide a means of determining

TABLE 5

HEATS OF ASSOCIATION CALCULATED FROM THE VARIATION OF β WITH TEMPERATURE

Vapour	β	T (°C.)	C_{v_0} (cal.mol.$^{-1}$)	$\Delta H_{calc.}$ (cal.mol.$^{-1}$)	$\Delta H_{expt.}$ (cal.mol.$^{-1}$)
Acetaldehyde	6·5 at 31 °C. $2{\cdot}1_5$ at 70 °C.	50	*c.* 12	4200	4600 (Lambert *et al.* 1949)
Methanol ..	10·9 at 79 °C. 4·3 at 110 °C.	94	*c.* 9·5	6300	6200 (Pauling 1944) *c.* 6000 (Weltner and Pitzer 1951)
Acetone ..	$2{\cdot}6_5$ at 98 °C. 2·0 at 110 °C.	104	*c.* 19	>5000*	

* Value uncertain because of small range of β values.

the heat of association. For if the equations are expressed in the form

$$\log \beta_{(d)} = -\log K_p + \log \text{ const. } \frac{(\Delta U)^2}{T^2 C_{v_0}},$$

a simple expression is obtained for the temperature dependence of β,

$$\frac{d[\log \beta_{(d)}]}{dT} = \frac{-\Delta H}{RT^2} + \frac{C_{v_0}}{(\Delta U)^2}\left[\frac{2\Delta U}{C_{v_0}} \cdot \frac{d(\Delta U)}{dT} - \frac{2(\Delta U)^2}{TC_{v_0}} - \frac{(\Delta U)^2}{C_{v_0}^2} \cdot \frac{dC_{v_0}}{dT}\right]$$

and from this expression ΔH, the heat of dimerization at constant pressure, may be derived. dC_{v_0}/dT is obtained from specific heat measurements, and if

the total specific heat of all molecules is regarded as independent of association, then from the Kirchhoff equation, $d(\Delta U)/dT$ is zero.

The equation reduces to

$$\frac{d[\log \beta_{(d)}]}{d(1/T)} = \frac{\Delta H}{R} + 2T + \frac{T^2}{C_{v_0}} \cdot \frac{dC_{v_0}}{dT}. \quad \ldots\ldots\ldots\ldots\ldots (5)$$

Values of ΔH obtained from equation (5) are given in Table 5; the small correction $170T_c^3/p_cT^3C_{v_0}$ has not been subtracted from the β values shown, since in the present calculation the corresponding change produced in ΔH is not large. For methanol and acetaldehyde there is fair agreement with values of ΔH obtained by other methods.

(*d*) *Energy Exchange and Heat Conduction*

An alternative explanation of the variation in conductivity of a vapour with change in pressure was put forward recently by Kannuluik and Donald (1950). These authors reported variations in the conductivities of methane, carbon dioxide, and nitrous oxide—of the order of 1 per cent./atm. at 0 °C.—and following a suggestion by Ubbelohde (1935) they tentatively attributed these effects to the hindered exchange of vibrational and translational energies within the vapours. Neither the present results nor the results of Lambert, Staines, and Woods provide any support for this conclusion, since for both carbon dioxide and methane the conductivity variations observed are very much less than those obtained by Kannuluik and Donald. Furthermore, such an effect should again be detected with organic vapours of rigid structure such as benzene for which, according to Lambert and Rowlinson (1950), the interchange of vibrational and translational energy is difficult. However, as may be seen from Table 1, the β values for benzene are no greater than those found for other non-polar organic compounds in which there is no appreciable barrier to energy exchange. The effect may be involved at lower pressures (cf. Schäfer, Rating, and Eucken 1942), as also may be the effect of variation of the accommodation coefficient of *vibrational* energy (Schäfer 1949), but it is evident that at the higher pressures of the present experiments the variation in conductivity of organic vapours with pressure cannot be attributed to any relaxation process.

V. Conclusions

The variation in thermal conductivity of organic vapours with pressure is related to the variation in the specific heats of the vapours with pressure. This is true for both polar and non-polar substances.

In the case of non-polar vapours the conductivity variation may be calculated using critical constants, from which the variation of specific heat with pressure can be obtained. For polar vapours a similar calculation is more complicated and involves the assumption of molecular association, although it is possible that this assumption is unnecessary and that the observed conductivity variations could be explained equally well in terms of dipole interaction. The calculated β values for different polar vapours are higher than the values obtained

by experiment; however, there is good agreement between the relative values. In this respect the present treatment is unlike that of Schäfer and Foz Gazulla (1942), from which β values are obtained of the same magnitude as those determined experimentally. Nevertheless, the treatment of Schäfer and Foz Gazulla is unsatisfactory on theoretical grounds, and a more rigorous theory of the transport properties of polar gases is required.

At ordinary pressures the hindered exchange of translational and vibrational energies in certain complex organic vapours has no apparent influence on the heat conduction.

VI. Acknowledgments

The author is grateful to Mr. J. D. Lambert and Dr. J. S. Rowlinson for helpful suggestions in the course of this research, and to Dr. S. D. Hamann and Dr. M. F. R. Mulcahy for useful criticism of the paper.

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Appendix I

The Validity of the Berthelot Equation

From a study of the Lennard-Jones equation, Lambert *et al.* (1949) showed that the second virial coefficient B, of a vapour, could be approximated by an equation containing a term of the inverse second power of the temperature. Within the temperature limits $T_c/T=0\cdot6$ and $T_c/T=4\cdot0$ the Berthelot expression for the virial coefficient was considered valid, except in the case of polar vapours for which the Lennard-Jones expression no longer applies.

More recently Guggenheim and McGlashan (1951) have pointed out that, according to the principle of corresponding states,

$$\frac{B}{V^*}=\varphi\left(\frac{T}{T^*}\right),$$

where φ is a universal function, and where V^* and T^* may conveniently be chosen as V_c the critical molar volume, and T_c the critical temperature. In Figure 8 values of B/V_c and T/T_c are plotted for various organic vapours, and are compared with curves given by the Lennard-Jones and Berthelot equations. For the vapours shown, the points fall close to both curves.*

The Lennard-Jones expression for the second virial coefficient is

$$\frac{B}{N}=\frac{2\pi D^3}{3}\sqrt{2}\left(\frac{\varepsilon^*}{kT}\right)^{\frac{1}{4}}\left\{\Gamma\frac{3}{4}-\sum_{n=1}^{\infty}\frac{2^{n-2}}{n\,!}\Gamma\left(\frac{2n-1}{4}\right)\left(\frac{\varepsilon^*}{kT}\right)^{\frac{1}{4}n}\right\},$$

where D is the molecular diameter, ε^* is the minimum interaction energy, and N is Avogadro's number. The tables of Hirschfelder, McClure, and Weeks (1942) were used to evaluate the Lennard-Jones function, and arbitrary values

$$\frac{\varepsilon^*}{kT_c}=0\cdot4025 \text{ and } \frac{2\pi D^3}{3}=3\cdot35\frac{V_c}{N},$$

were chosen to give agreement with the experimental points at $T/T_c=0\cdot6$ and $0\cdot85$.

The Berthelot formula written as a reduced equation is

$$\frac{B}{V_c}=0\cdot464-1\cdot625\left(\frac{T_c}{T}\right)^2, \quad \ldots\ldots\ldots\ldots\ldots\ldots \quad (6)$$

with the constants again adjusted to give a good fit with experimental points at $T/T_c=0\cdot6$ and $0\cdot85$. It is seen that in the range from $T/T_c=0\cdot5$ to $1\cdot0$ the Berthelot equation is in no way inferior to the Lennard-Jones function. This provides some justification for using a formula of the Berthelot type in evaluating equation (1).

Values for the second virial coefficient B, calculated from equation (6), differ very little from values calculated from the reduced Berthelot expression which for most organic vapours is

$$\frac{B}{V_c}\simeq0\cdot25-1\cdot5\left(\frac{T_c}{T}\right)^2.$$

* Points for highly polar vapours such as methanol, acetonitrile, and amines other than the tertiary amines, all lie considerably below the curves. With methyl chloride the deviations, although still apparent are not so marked, and points for ether, chloroform, and carbon tetrachloride fit well except at lower temperatures.

This expression contains constants intermediate in value between those of equation (**6**) and those of the equation of best fit at higher temperatures :

$$\frac{B}{V_c} = 0 \cdot 196 - 1 \cdot 396 \left(\frac{T_c}{T}\right)^2$$

(cf. Guggenheim and McGlashan 1951). For this reason the conventional formula has been used in the evaluation of equation (**1**) ; whichever expression is used the values of $\beta_{calc.}$ in Table 3 differ by only about 10 per cent., which is negligible as far as comparison with $\beta_{obs.}$ is concerned.

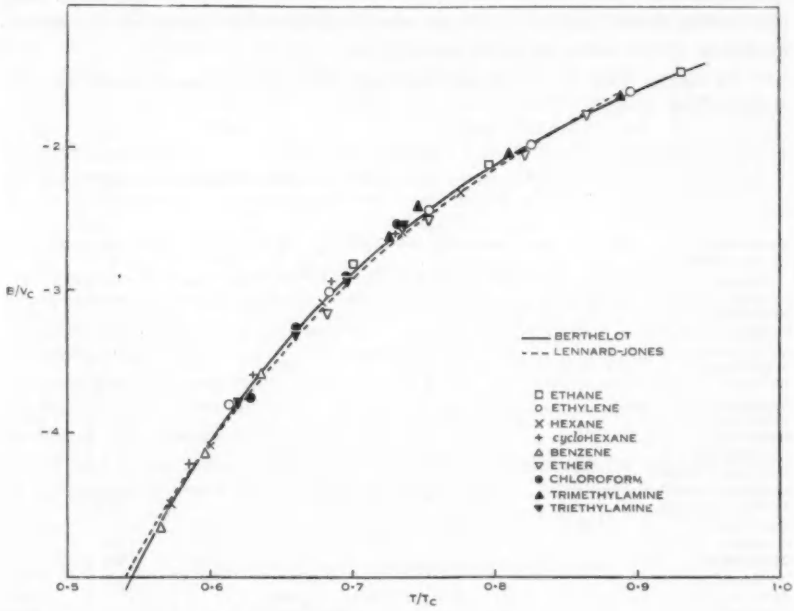

Fig. 8.—Reduced virial coefficients of organic vapours. Values for B from the measurements of Lambert *et al.* (1949) and values for V_c and T_c from Landolt-Börnstein. V_c for hexane was taken as 391 cc./mole.

Appendix II

The Variation of Conductivity with Temperature

In the equation

$$\frac{K^\circ_{\text{vap.}}}{K^\circ_{\text{air}}} = \frac{I^2_{0\,\text{vap.}}}{I^2_{0\,\text{air}}},$$

from which the absolute vapour conductivities are determined, the values of $I^2_{0\,\text{air}}$ are obtained by extrapolation. As has been shown, the β values for air are

largely due to accommodation effects, and the extrapolated values of $I^2_{0\,air}$ are consequently too small and the absolute conductivities of the vapours correspondingly too high. In the present measurements the error is less than $\frac{1}{2}$ per cent., but with the apparatus of Lambert, Staines, and Woods where accommodation effects were more pronounced, the results may be high by more than 1 per cent. The conductivity values shown in Figures 3–6 should thus be decreased by about 0·3 per cent. at 30 °C., 0·35 per cent. at 70 °C., and 0·4 per cent. at 110 °C., and the results of Lambert *et al.* by about 0·7 per cent. at 31 °C., 0·9 per cent. at 66 °C., and 1·3 per cent. at 85 °C. Under these conditions comparison of the measurements is possible. The adjusted results are tabulated below. The values for carbon dioxide and argon have been obtained as above, and no additional corrections have been made for the accommodation effects observed with these gases.

All results have been referred to Kannuluik and Carman's values for the conductivity of air.

TABLE 6

THE VARIATION OF THE THERMAL CONDUCTIVITIES OF ORGANIC VAPOURS WITH TEMPERATURE

$K^\circ \times 10^6$ (cal. cm.$^{-1}$ sec.$^{-1}$ deg.$^{-1}$)

Temperature (°C.)	30·9	* 31·2	45·1	55·6	* 65·9	69·6	75·0	79·1	* 85·0	87·0	98·0	100·7	109·4	109·8	110·1
Air (Kannuluik and Carman) ..	62·9	63·0	65·5	67·1	68·9	69·5	70·3	71·0	72·1	72·3	74·1	74·6	75·8	75·9	76·0
Nitromethane ..															31·7
Methanol					43·4$_5$			47·0$_5$	48·5$_5$					54·4$_5$	
tert.-Butanol ..														53·8	
Acetaldehyde ..	28·3	28·6$_5$	31·1$_5$		35·0	35·8			39·0$_5$		41·3$_5$				
Diacetyl													42·0		
Acetone					34·7		36·4$_5$		38·4		41·0$_5$		43·8		
Ethyl acetate ..											40·4				43·9
Methyl acetate ..						35·8$_5$					41·8				
Ethyl formate ..						36·7$_5$					43·3				46·8
Methylene bromide															17·8
Ethylidene chloride						26·6					30·7		32·5		
Ethylene dichloride													31·9$_5$		
Ethyl chloride ..		27·3			33·6$_5$	34·0			37·2		39·5				42·2$_5$
Chloroform ..					20·4$_5$		21·4		22·2$_5$		23·6		25·0		
Diethylamine ..						44·3$_5$					51·5		54·7$_5$		
Triethylamine ..											45·5$_5$		48·6		
Ether					44·2		46·5$_5$		48·8						56·0$_5$
Thiophene															36·4$_5$
Benzene					31·7		33·7		35·9						41·7$_5$
Hexane					39·4$_5$		41·7		44·1					50·6	50·8
*cyclo*Hexane ..					35·4$_5$		37·6	38·8$_5$	40·2$_5$			44·2			46·5
Carbon dioxide (impure)	39·5			44·2$_5$	46·5$_5$				50·1$_5$	50·4$_5$					
Argon (impure) ..															51·6$_5$

* Values of Lambert *et al.*

In Figure 7 the conductivity values for various vapours in Table 6 have been plotted against temperature. The conductivity of a vapour at zero pressure is given by

$$K^\circ = \text{const. } \eta_l C_{v_0}/M,$$

where η is the viscosity, C_{v_0}/M the specific heat of the vapour, and the constant involved is the Eucken factor approximately equal to $1+4\cdot47/C_{v_0}$ (Eucken 1913 ; cf. however, Schäfer 1943). The viscosities of organic vapours are proportional to the temperature over a large temperature range (Craven and Lambert 1951) so that

$$K^\circ = aC_{v_0}T + bT,$$

where a and b are constants. Thus

$$\frac{dK^\circ}{dT} = aC_{v_0} + aT \cdot \frac{dC_{v_0}}{dT} + b.$$

This equation implies firstly that the increase in conductivity with increasing temperature is greater for vapours of large specific heat (see Table 2). Secondly, since dC_{v_0}/dT is positive, the conductivity increases with temperature at a more than linear rate. Over the small temperature range involved in the present experiments the variation of conductivity with temperature is approximately linear ; however, careful inspection of the points in Figure 7 shows the expected positive deviations. It is clear from Figure 7 that the present results are in accord with the earlier results of Lambert *et al.*

Appendix III

Conductivities of Vapour Mixtures

Preliminary experiments have been carried out using a 50/50 vapour mixture of ether and chloroform. These substances combine when mixed as liquids (Dolezalek and Schulze 1913 ; cf. however, Hildebrand and Scott 1950), and in the vapour phase association by hydrogen bonding might be expected. Further evidence on this point has been provided by the recent virial coefficient measurements of Fox and Lambert (1951).

The β values obtained are shown in Table 7. Although unequal adsorption in the apparatus alters the composition of the mixture as the pressure is changed,

Table 7

β values of 50/50 ether-chloroform mixture

β Value of : \ Temperature (°C.)	75	110
Mixture	6·0	1·9
Components alone	c. 1·3	c. 0·9

the β values obtained are surprisingly reproducible. The errors in the measurements may be considerable, but qualitatively they provide further evidence that strong interaction between the molecules in a vapour can cause a change in the conductivity of the vapour with pressure.

Appendix IV

Purification of Compounds Used

(i) *Gases*

Air was freed from water vapour and carbon dioxide by passing through bubblers of sulphuric acid, and then through towers of solid potassium hydroxide and phosphorus pentoxide.

Carbon Dioxide.—A cylinder of commercial carbon dioxide (sulphur free) was up-ended and a considerable portion blown off. Gas was then taken directly from the cylinder.

Methane.—It was not necessary for the methane to be completely pure as the measurements with this gas were only exploratory. Gas from a cylinder of " pure " methane (Matheson) was condensed in liquid air and distilled in a vacuum several times, the end fraction being discarded.

Argon was taken directly from a cylinder stated to be 98 per cent. pure.

(ii) *Liquids*

All liquids were frozen in liquid air in a bulb attached to the apparatus ; they were vacuum distilled into a second bulb, the middle fraction being collected, and were refrozen and pumped out before being used.

Benzene was shaken with concentrated sulphuric acid, washed with water, dried over calcium chloride, and distilled.

cyclo*Hexane* was shaken with concentrated sulphuric acid, again with concentrated nitric acid, and distilled. It was then dried over potassium carbonate and redistilled.

Hexane.—Phillips (Oklahoma, pure grade) stated to be better than 99 per cent. pure was used without further purification.

Ether.—" Analar " ether was shaken with ferrous sulphate and distilled. It was dried over calcium chloride and stored over sodium.

Chloroform was shaken with concentrated sulphuric acid, washed, and dried over potassium carbonate before distilling.

Methanol was refluxed with magnesium and a trace of iodine and distilled.

tert.-*Butanol* was purified by fractional crystallization.

Ethyl acetate and other esters were washed with sodium carbonate, dried with potassium carbonate, and distilled.

Acetone.—" Analar " acetone was dried over potassium carbonate and distilled.

Nitromethane was dried over calcium chloride and distilled.

Diethylamine and triethylamine were dried with solid potassium hydroxide and carefully fractionated on distillation.

Ethyl Chloride.—Ethyl chloride anaesthetic was used without further purification.

All other compounds were distilled and purified by vacuum distillation as already described.

DIELECTRIC ANISOTROPY IN CRYSTALLINE LONG-CHAIN ALCOHOLS

By B. V. Hamon* and R. J. Meakins*

[*Manuscript received September* 4, 1952]

Summary

Pressed disks made from powdered crystalline long-chain *n*-primary and secondary alcohols have been shown to be electrically anisotropic. At a particular frequency, the loss factor, when the applied field is parallel to the faces of the disk, is from two to five times greater than when the field is perpendicular to the faces. The observed anisotropy is considered to be due to orientation of the flat crystals of the alcohols parallel to the disk faces.

The effect of anisotropy on previously published results for long-chain compounds is discussed. The observed anisotropy is consistent with the main conclusions from this earlier work. The application of the measuring technique to other materials is suggested.

I. Introduction

The work described in the present paper arose from the investigation of discrepancies between the dielectric properties of *n*-primary alcohols when measured with different electrodes. It was found that samples allowed to solidify in a rhodium-plated cell (Hamon and Meakins 1952) showed an absorption about twice as great as disks prepared from the same material by allowing it to solidify in a beaker, then crushing with a mortar and pestle, and pressing in a mould. It is known that differences are to be expected between materials recrystallized from a solvent and the same material solidified from the melt (see, for example, Meakins and Sack 1951) but in the above case both samples had been solidified from the melt. It was thought at first that the discrepancy may have been due to orientation of the crystals during their formation in the cell, since orientation in long-chain compounds solidified at metal surfaces has been found in X-ray work (Müller and Lonsdale 1948). As will be shown, however, this effect appears to be negligible for the relatively thick samples used here. A satisfactory explanation for the discrepancy was found in the existence of a marked degree of orientation in the pressed samples.

The experimental method that appeared most suitable for investigating anisotropy was to cut square bars from disk samples (Fig. 1) and measure their electrical properties in two mutually perpendicular directions. Since material solidified in the rhodium-plated cell could not be removed for preparation in this form, cast disks were prepared by allowing the material to solidify on a mercury surface, and bar samples were cut from these disks.

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II. Experimental Methods

(*a*) *Materials*

The preparation and purification of the materials used have been described in earlier papers (Meakins and Sack 1951 ; Hamon and Meakins 1952).

(*b*) *Preparation of Samples*

Each sample was first made in the form of a flat disk, either by casting on mercury or pressing in a mould. The cast samples were about 6·5 cm. in diameter and 0·2 cm. thick. They were made by melting the material and pouring it onto the surface of clean mercury that had previously been heated to a

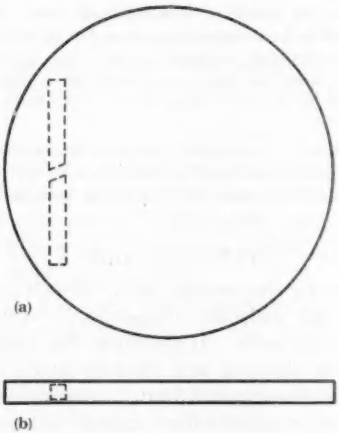

Fig. 1.—Position of square bar samples in relation to the original cast or pressed disk. (*a*) Plan. (*b*) Elevation.

temperature above the melting point of the material. The material was solidified by placing the dish containing the mercury on a cool metal plate.

The pressed samples were 5 cm. in diameter and 0·2 cm. thick. They were prepared either from crystals obtained by recrystallization from a suitable solvent (" recrystallized " material) or by using material that had been melted, allowed to solidify, and then crushed with a mortar and pestle (" melted " material).

After measuring the electrical properties of each disk, two bars of square cross section were cut from the disk. Figure 1 shows the position of the bars in relation to the original disk. The bars were cut initially with a small metal hack-saw blade, and then shaved to final size and shape with a razor blade. A simple jig of sheet plastic was used to hold the bars during the shaping process. The finished dimensions of each bar were $0 \cdot 183 \pm 0 \cdot 003$ cm. square, and 0·95 cm. long.

(c) *Electrodes*

The disk samples were measured between mercury electrodes of the type described by the Electrical Research Association (1933).

The two square bars from each disk were measured side by side between amalgamated copper surfaces as shown in Figure 2.

After measuring with one orientation, the bars were turned through 90° about their long axes and remeasured. This process was repeated a few times to make sure that the results were not being affected by contamination of the vertical surfaces.

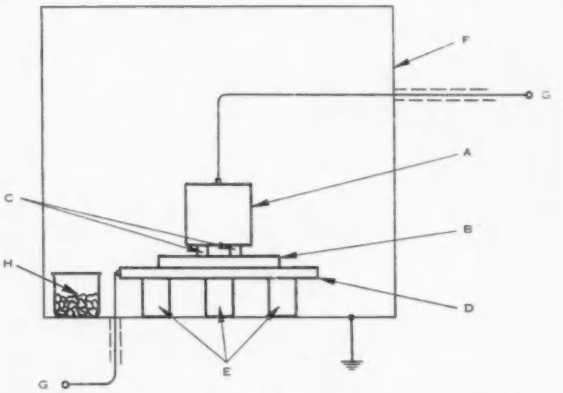

Fig. 2.—Electrode arrangement for measuring square bar samples.
A, *B*, electrodes; *C*, sample; *D*, supporting plate; *E*, insulators; *F*, shield; *G*, leads to measuring equipment; *H*, calcium chloride.

(d) *Measuring Apparatus*

Measurements between 5 c/s. and 100 kc/s. were made with a permittivity and power-factor bridge designed in this Laboratory (Thompson, unpublished data). A three-terminal piston capacitor with a range 1–6 μμF. was used with the bridge for measuring the bar samples. The sensitivity was such that 0·001 μμF. could be detected. A Schering bridge with Lindemann electrometer as detector was used at frequencies between 0·4 and 4 c/s. The loss factors at lower frequencies were deduced from the charging current following a suddenly applied D.C. potential (Hamon 1952).

The stray capacitance in parallel with the bar samples was determined by measuring bars of identical dimensions cut from a paraffin wax disk.

III. Results

(a) *Pressed Samples*

(i) *Recrystallized Material.*—Figure 3 shows the results obtained on square bar samples of recrystallized *n*-hexadecyl alcohol. In making the disk from which these samples were cut, an attempt was made to get as high a degree

of orientation as possible. *n*-Hexadecyl alcohol recrystallized slowly from benzene was used, since larger crystals are formed from this solvent than from methanol or ethanol. After filtering and vacuum drying, the recrystallized material was in the form of large polycrystalline plates, which packed into the mould with a high degree of orientation. In the square bars cut from the pressed disk, this orientation could still be detected by the different appearance of adjacent faces.

It will be seen from Figure 3 that the loss factor is about five times larger when the applied field is parallel to the faces of the original disk. The factor of 5 is approximately independent of frequency from D.C. to 100 kc/s.

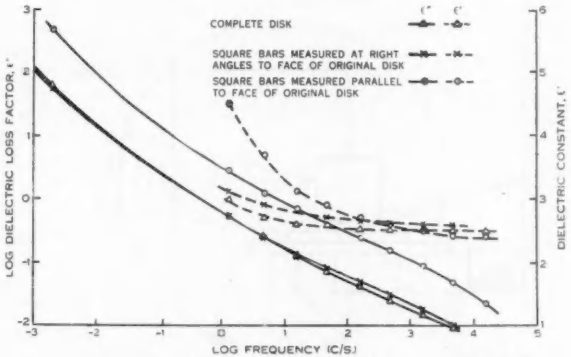
COMPLETE DISK
SQUARE BARS MEASURED AT RIGHT ANGLES TO FACE OF ORIGINAL DISK
SQUARE BARS MEASURED PARALLEL TO FACE OF ORIGINAL DISK
LOG DIELECTRIC LOSS FACTOR, ε''
DIELECTRIC CONSTANT, ε'
LOG FREQUENCY (C/S)

Fig. 3.—Dielectric anisotropy of recrystallized *n*-hexadecyl alcohol.

To check the accuracy of measurement on the small bar samples the results for the complete disk are also given in Figure 3. These show satisfactory agreement with the values obtained on the bars when the applied field is perpendicular to the faces of the original disks. Exact agreement is not to be expected, since the orientation is not likely to be uniform throughout the disk.

Similar results were obtained with two recrystallized secondary alcohols (10-nonadecanol and 14-heptacosanol). Since the losses in the recrystallized forms of secondary alcohols are small at all frequencies (Meakins and Sack 1951), the accuracy of measurement of the bar samples was very low, but the measurements showed definitely that the loss in the parallel direction was three or four times greater than in the perpendicular direction.

(ii) *Melted Material.*—Measurements were also made on square bar samples of a primary alcohol (*n*-hexadecyl) and a secondary alcohol (14-heptacosanol) cut from disks prepared from melted material. It was again found that the loss factor with the field parallel to the faces of the disk was larger than that obtained with the field perpendicular to the faces. The ratio of loss factor values in the two directions at a particular frequency was about two for the *n*-hexadecyl alcohol, and about four for the 14-heptacosanol. The results for the 14-heptacosanol are shown in Figure 4. The degree of anisotropy shown by these samples

is surprising at first sight, since the crushed material did not appear flaky. Microscopic examination showed, however, that even after prolonged grinding many of the alcohol particles were in the form of small flakes, and it is presumed that these flakes tend to orient parallel to the disk faces during the pressing. This behaviour is apparently not common to all long-chain materials, since disks of hexamethylene glycol and the ester cetyl palmitate, prepared by grinding and pressing melted material, were found to be isotropic.

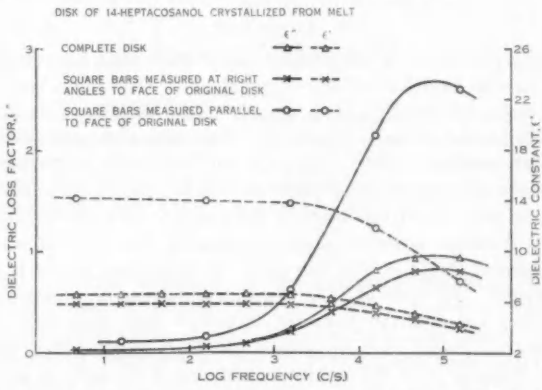

Fig. 4.—Dielectric anisotropy of 14-heptacosanol disk, melted form.

(*b*) *Cast Samples*

Bar samp es cut from cast disks of *n*-hexadecyl alcohol, *n*-dodecyl alcohol, and 14-heptacosanol showed only a small degree of anisotropy. The difference between loss factors in the two directions was about 20 per cent. in each case. In contrast to the pressed samples, the loss factor was found to be larger in the perpendicular direction. Microscopic examination of broken edges of cast disks showed that the crystals formed near the mercury surface tended to be oriented perpendicular to the surface. This would account for the change in the direction of the anisotropy in the cast samples compared with the pressed samples. The smaliness of the effect in the cast samples may be due to a decrease in the amount of orientation with increasing distance from the mercury surface.

IV. Discussion

(*a*) *Effect on Previous Results*

The anisotropy in pressed disks of primary and secondary alcohols has been shown to be very large compared with the accuracy of measurement of the properties of a particular sample. Since this anisotropy was not suspected until recently, some of the results published in earlier papers from this Laboratory can be expected to be in error from this cause. In general, the loss factors and dielectric constants for long-chain materials pressed from melted or recrystallized material can be expected to be low compared with the values to be expected for randmoly oriented material. An examination of previous papers with this

point in mind, however, has shown that the main conclusions are not affected by errors due to anisotropy, and that the loss mechanisms suggested are consistent with the present observations. The large differences between melted and recrystallized material in secondary alcohols (Meakins and Sack 1951), DL-*n*-eicosanols (Meakins and Welsh 1951) and, to a lesser extent, primary alcohols (Meakins and Mulley 1951) are not appreciably reduced when the probable effects of anisotropy are taken into account.

V. Conclusion

The results presented in the present paper show that appreciable dielectric anisotropy exists in samples of long-chain alcohols that have been prepared in the form of disks by pressing in a mould. The anisotropy is greatest when recrystallized material is used, but is still large when the material is prepared for pressing by melting, solidifying, and crushing with a mortar and pestle. The existence of anisotropy in long-chain alcohol samples may cause the measured loss factor to be only about one-third of the value to be expected in an isotropic sample. This fraction, however, is approximately the same at all frequencies, so that the general shape of the loss factor $v.$ frequency curve is not changed by the anisotropy. In view of this, the continued use of pressed disk samples for investigating the relation between structure and dielectric properties of materials appears to be justified, but care is necessary in comparing quantitatively the results so obtained with the results on samples of the same material prepared in a different way, or with theoretical values.

Anisotropy can be expected in bulk samples of other compounds if, firstly, their individual crystals are anisotropic and secondly, the crystals have growth habits or cleavage planes resulting in crystal shapes that orient easily. Where the anisotropy can be related to crystal structure, useful information on the relation between dielectric properties and structure may be obtained. The technique described in this paper may prove useful in cases of this kind, especially if single crystals of suitable size cannot be grown.

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THE VIBRATIONAL SPECTRA OF METHANE SULPHONYL CHLORIDE AND METHANE SULPHONYL FLUORIDE

By N. S. Ham* and A. N. Hambly†

[*Manuscript received October* 9, 1952]

Summary

The Raman and infra-red spectra of methane sulphonyl chloride and methane sulphonyl fluoride have been measured. Assignments of the vibrational frequencies of the two molecules have been made; the frequency 377 cm.$^{-1}$ is characteristic of the S—Cl linkage and 1210 cm.$^{-1}$ of the S—F linkage in these compounds. An improved method for the preparation of methane sulphonyl fluoride is described.

I. Introduction

The general chemical inertness of the sulphonyl fluorides compared to the other sulphonyl halides (Suter 1944) indicates a powerful bonding force between the sulphur and fluorine atoms. This bond strength should be correlated with a high stretching frequency of the S—F bond and therefore the Raman and infra-red spectra of methane sulphonyl chloride and methane sulphonyl fluoride were determined and compared.

II. Experimental

Methane sulphonyl chloride was prepared according to the method of Johnson and Sprague (1936). The distilled product, b.p. 62 °C./20 mm., was redistilled directly into the specimen tube of the Raman apparatus. Methane sulphonyl fluoride was prepared by the method set out in Appendix I and was also distilled into the specimen tube of the apparatus.

Raman spectra were obtained by exposing the sample, surrounded by a filter jacket containing dilute potassium chromate or saturated sodium nitrite solution, to the radiation from four commercial 400 W. mercury lamps. The assembly was surrounded by a cylindrical reflector smoked with magnesium oxide which has a reflectivity of 98 per cent. at 4360 Å (Menzies and Skinner 1949). The specimen tube (capacity 25 ml.) had an optical flat sealed to the end and the scattered light was focused onto the slit by a cylindrical lens, of the same aperture as the spectrograph (f/10). The spectrograph was a Hilger "medium" type fitted with a glass train. Tracings from the plates were obtained on a Leeds-Northrup recording microphotometer and the dispersion curve of the spectrograph by measurements of tracings of an iron arc. Raman frequencies could be measured with a reproducibility of ± 1 cm.$^{-1}$ for strong, sharp bands and ± 3 cm.$^{-1}$ for weak or diffuse bands.

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TABLE 1

VIBRATIONAL ASSIGNMENT FOR CH_3SO_2Cl

Infra Red	Raman	Assignment
	216 (w.)	Skeletal out-of-plane bend
	257 (m.)	Skeletal in-plane bend
	288 (m.)	Skeletal in-plane bend
	377 (v.v.s.)	S—Cl stretch
490 (s.)	486 (s.)	Skeletal in-plane bend
528 (m.)	538 (s. diff.)	S—O deformation
751 (s.)	748 (m.)	C—S stretch
	811 (w.)	CH_3 out-of-plane wag
968 (s.)	966 (w.)	CH_3 in-plane wag
1081 (v.v.w.)		1367—288
1175 (v.s.)	1168 (v.s.)	S—O sym. stretch
1324 (s.)		C—H sym. deformation
1367 (v.s.)	1361 (m. diff.)	S—O asym. stretch
1411 (m.s.)	1409 (m. diff.)	C—H asym. deformation (2)
2076 (v.w.)		1324+751
2305 (w.)		1324+968
2345 (v.w.)		1175+1175
2567 (w.)		1175+1411
2950 (m.)	2933 (s.)	C—H sym. stretch
3045 (m.)		C—H asym. stretch (2)

TABLE 2

VIBRATIONAL ASSIGNMENT FOR CH_3SO_2F

Infra Red	Raman	Assignment
	326 (m.)	C—S—F skeletal bend
	350 (w.)	Skeletal out-of-plane bend
462 (s.)	457 (w.)	Skeletal in-plane bend
493 (s.)	493 (m.)	Skeletal in-plane bend
534 (v.s.)	531 (s.)	S—O deformation
733 (s.)	738 (v.v.s.)	C—S stretch
813 (s.)	809 (v.w.)	CH_3 out-of-plane wag
985 (m.)		CH_3 in-plane wag
1177 (w.)	1186 (v.s.)	S—O sym. stretch
1210 (v.s.)	1210 (v.s.)	'S—F stretch'
1341 (m.)	1341 (w.)	C—H sym. deformation
1396 (v.s.)	1401 (m.)	S—O asym. stretch
1425 (s.)	1410 (m.)	C—H asym. deformation (2)
2080 (w.)		1341+733
2160 (v.w.)		1425+733
2330 (w.)		1341+985
2955 (w.)	2952 (v.v.s.)	C—H sym. stretch
3045 (w.)		C—H asym. stretch (2)

The infra-red spectra were determined with a Perkin-Elmer 12C infra-red spectrometer using sodium chloride (2–15μ) and potassium bromide (15–25μ) prisms. A layer of liquid of indefinite thickness between two potassium bromide plates constituted the sample.

The frequencies and relative intensities observed in the Raman and infra-red spectra are shown in Tables 1 and 2.

III. Assignment of Spectra

The most reasonable structure for the sulphonyl halide group is tetrahedral with the sulphur atom at the centre of the tetrahedron. This assumption is based on the electron diffraction data for sulphuryl chloride, SO_2Cl_2 (Yost and Russell 1944), and Raman spectrum studies with pyrosulphuryl chloride, $S_2O_5Cl_2$ (Gerding and Linden 1942), which show such an arrangement in both these molecules. If it is also assumed that there is free rotation about the C—S bond, then the only element of symmetry in the methane sulphonyl halide molecule is a plane of symmetry. The molecule thus belongs to the C_s point group and all the fundamental vibrations should occur in both the Raman and infra-red spectra. The molecule $CH_3.SO_2X$ has 18 fundamental vibration frequencies which would be expected to consist (on analogy with similar molecules (Sheppard 1949*a*, 1949*b*)) of two asymmetrical and one symmetrical C—H stretching modes; one asymmetrical and one symmetrical S—O stretching modes; two asymmetrical and one symmetrical C—H deformation modes; one S—O deformation mode; methyl group in-plane and out-of-plane wagging modes; C—S stretching mode; S—X stretching mode; four skeletal bending modes and one mode representing the restricted rotation about the C—S bond.

(*a*) *Methane Sulphonyl Chloride*

The Raman spectra of some simple inorganic compounds containing the $-SO_2$ grouping (Hibben 1939) and the infra-red spectra of some sulphones (Schreiber 1949) show that the two frequencies associated with this grouping lie in the regions 1150–1190 cm.$^{-1}$ for the symmetrical stretch and 1320–1390 cm.$^{-1}$ for the asymmetrical S—O stretch. Since symmetrical frequencies are usually strong in Raman scattering and asymmetric frequencies are strong in absorption, the symmetrical and asymmetrical S—O stretching modes in methane sulphonyl chloride are assigned to 1168 and 1367 cm.$^{-1}$ respectively. The S—O deformation frequency is 538 cm.$^{-1}$ (this occurs at 519 cm.$^{-1}$ in sulphur dioxide).

Sheppard (1950) from a study of the infra-red spectra of mercaptans, sulphides, and disulphides concluded that the C—S frequency occurs in the range 600–700 cm.$^{-1}$, while Houlton and Tartar (1938) assign a frequency, which occurs at 760–790 cm.$^{-1}$ in the Raman spectra of the sodium salts of alkyl sulphonates, to this vibration. The band at 748 cm.$^{-1}$ is therefore assigned to the C—S stretching vibration.

Raman and infra-red studies of simple sulphur chlorine compounds show a frequency in the neighbourhood of 400 cm.$^{-1}$ which is associated with the S—Cl stretching vibration. The strong Raman band at 377 cm.$^{-1}$ is attributed to

this vibration in the sulphonyl chloride. This frequency is absent from the methane sulphonyl fluoride spectrum.

The six frequencies due to the internal motions of the methyl group and the two wagging modes 968, 811 cm.$^{-1}$ are assigned by comparison with those found in the related molecules ethyl mercaptan, acetyl chloride, and thioacetic acid. The four remaining frequencies below 500 cm.$^{-1}$ are apparently the four skeletal bending modes of the molecule. The vibration involving restricted rotation about the C—S linkage is not observed, and five weak infra-red bands are reasonably accounted for in terms of combinations of the fundamentals already assigned.

(*b*) *Methane Sulphonyl Fluoride*

It is to be expected that the vibration spectrum of methane sulphonyl fluoride would be very similar to that of the chloride except that the S—Cl stretching frequency would be replaced by one characteristic of the S—F linkage. The significant change is the disappearance of the strong band at 377 cm.$^{-1}$ in the chloride and the appearance of a strong band at 1210 in both the infra-red and Raman spectra of the fluoride. This frequency is also present in the spectra of a series of aromatic sulphonyl fluorides (Ham 1951). The series shows no other common line which could be assigned to the S—F stretch.

Although it was expected that the stretching frequency of the S—F bond would be high, due to effects related by Pauling (1944) to " partial double bond " character of such linkages, the value of 1210 cm.$^{-1}$ is greater than is probable for this bond. In addition the S—F bond is expected to be strongly polarized and to give a strong infra-red absorption band but a weak band in the Raman spectrum. The band at 1210 cm.$^{-1}$ is however strong in both spectra. The symmetrical " breathing " frequency of the octahedral sulphur hexafluoride molecule was found by Yost, Steffans, and Gross (1934) and Eucken and Ahrens (1934) at 775 cm.$^{-1}$ while Yost (1938) found the symmetric and asymmetric S—F stretching modes of thionyl fluoride at 720 and 790 cm.$^{-1}$. On this evidence it appears that the 1210 cm.$^{-1}$ frequency is characteristic of the $-SO_2F$ grouping but is not a simple S—F stretching vibration.

The asymmetric S—O stretching frequency is increased in methane sulphonyl fluoride to 1401 cm.$^{-1}$. A similar increase is observed in the S—O stretching frequency of the thionyl halides which occurs at 1229 cm.$^{-1}$ in the chloride and at 1312 cm.$^{-1}$ in the fluoride. The greater electronegativity of fluorine reduces the ionic character of the S—O bond and increases its covalent nature (Barnard, Fabian, and Koch 1949).

IV. Acknowledgments

The authors express their thanks to Dr. A. L. G. Rees, Division of Industrial Chemistry, C.S.I.R.O., Melbourne, for the use of the microphotometer and the infra-red spectrometer, and to Mr. A. Walsh and Dr. J. B. Willis for helpful discussions.

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Appendix I

Preparation of Methane Sulphonyl Fluoride

Davies and Dick (1932) prepared methane sulphonyl fluoride by heating methane sulphonyl chloride with anhydrous zinc fluoride in a platinum vessel for 18 hr. We find that this compound can be prepared in good yield by a method similar to that employed by Davies and Dick for ethane sulphonyl fluoride, providing that the reaction temperature is kept below 10 °C. in order to slow down the competing hydrolysis reaction. The latter has a higher energy of activation than the fluorolysis reaction (Bradbury and Hambly, unpublished data) so that the fluorolysis reaction is still rapid at this temperature.

Methane sulphonyl chloride 22·8 g. (0·2 mole) was shaken vigorously with a saturated aqueous solution, containing 23·2 g. (0·4 mole) of potassium fluoride, for 25 min. in an ice-bath—when the odour of the sulphonyl chloride was no longer detectable. The mixture was diluted with water to dissolve the precipitated potassium chloride and extracted with ether. The ether extract was washed once with water and dried over anhydrous $CaCl_2$. The ether was distilled off and then the sulphonyl fluoride distilled under reduced pressure. The sample for spectroscopic study was redistilled at atmospheric pressure through a short column. The product 13·5 g. (69%) had b.p. 80 °C. (40 mm.); 124 °C. (760 mm.) and the molecular weight, determined by hydrolysis with standard alkali, was 98·04 (theor. 98·09).

THE CHEMISTRY OF QUINONES

I. DIRECTIVE EFFECTS IN THE SUBSTITUTION OF NAPHTHOQUINONES

By R. G. Cooke,* H. Dowd,* and W. Segal*

[*Manuscript received September 22, 1952*]

Summary

The reaction of dimethylamine with 5-methoxy-1,4-naphthoquinone gives approximately equal amounts of the two possible substitution products and with 6-methyl-1,4-naphthoquinone followed by acid hydrolysis 2-hydroxy-6-methyl-1,4-naphthoquinone is the principal product. Similar treatment of 5-methyl-1,4-naphthoquinone gives mostly 3-hydroxy-5-methyl-1,4-naphthoquinone. The isomer, 2-hydroxy-5-methyl-1,4-naphthoquinone, has been prepared by another method. The product of Thiele-Winter addition of acetic anhydride to juglone is shown to be a mixture of the two possible isomers, but authentic 1,3,4,5-tetra-acetoxynaphthalene has been prepared from 3,5-dihydroxy-1,4-naphthoquinone. The reaction of acetic anhydride with plumbagin gives three compounds, the composition of the mixture depending on the time of contact. Juglone and plumbagin have been selectively brominated in the 6-position and certain other halogen derivatives of these quinones have been prepared. The preparation of 3-chloro-5-hydroxy-2-methyl-1,4-naphthoquinone provides a new route by which droserone may be obtained from plumbagin.

I. Introduction

Substitution reactions in the quinonoid ring of juglone and some of its derivatives are known to be influenced by the nature of the substituents already present in the benzenoid ring. Usually one of the two possible isomeric products predominates, and in many cases exclusive formation of one isomer has been claimed. Cooke and Segal (1950) and Thomson (1951*a*) have attempted to account for these results in terms of electronic effects relayed from the 5-substituent.

The isolation of only one isomer from substitutions of juglone acetate is not readily explained since no strong specific activation or deactivation would be expected from the 5-acetoxy-group. However, in some cases the reported yield of substitution product is only moderate and the formation of substantial amounts of the second isomer is not excluded. The ready hydrolysis of the acetoxy-group is a factor which may confuse the issue in some cases, and in particular it limits the investigation of substitution by bases. It was therefore considered necessary to determine the effects of other substituents which would be expected to give results similar to those of the acetoxy-group.

(*a*) *Reaction with Dimethylamine*

The reaction of dimethylamine with 5-methoxy-1,4-naphthoquinone and with 5- and 6-methyl-1,4-naphthoquinone has been studied. The methoxy-

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and methyl substituents were chosen for their stability and because they would be more likely to give specific directive effects of the kind previously claimed for the acetoxy-group.

No attempt was made to isolate the primary products of substitution but the crude dimethylaminoquinones were hydrolysed to the corresponding hydroxyquinones. The latter are generally more readily purified, and the orientation of substituents is more readily determined.

The two isomeric products from 5-methoxy-1,4-naphthoquinone were apparently formed in approximately equal amounts, but they could not be separated easily. However, after demethylation the known 2,5-dihydroxy-1,4-naphthoquinone was obtained, while the action of diacetyl peroxide gave a mixture of products from which 2-methyl-3-hydroxy-5-methoxy-1,4-naphthoquinone was readily separated.

Only one pure compound was obtained from 5-methyl-1,4-naphthoquinone, but there was some evidence of the presence of a small amount of the other isomer. The product was evidently 3-hydroxy-5-methyl-1,4-naphthoquinone since it was not identical with 2-hydroxy-5-methyl-1,4-naphthoquinone prepared from 5-methyl-1-tetralone by the general method of Buu-Hoï and Cagniant (1942).

From 6-methyl-1,4-naphthoquinone only the known 2-hydroxy-6-methyl-1,4-naphthoquinone was isolated, but again there was some evidence of the formation of small amounts of the other isomer.

These results suggest that the acetoxy-group should not have any strong directive effect in substitution reactions of this type. However, the predominant formation of one isomer from each of the methylnaphthoquinones is in accord with the earlier suggestions concerning the effect of a predominantly electron-releasing substituent.

It seemed possible that previous reports of the formation of only one isomer from juglone acetate may have been due in some cases to the difficulty of separating and purifying the products. This does account for at least one such claim, as the following results show.

(*b*) *Thiele-Winter Addition Reaction*

Fieser and Dunn (1937) and Thomson (1951*a*) have reported that the addition of acetic anhydride to juglone acetate gives only one product, and Thomson claimed that this was 1,3,4,5-tetra-acetoxynaphthalene. It has now been found that this product actually consists of approximately equal amounts of the two possible isomers. Hydrolysis and oxidation gave a considerable amount of 2,5-dihydroxy-1,4-naphthoquinone, which was isolated as the diacetate. Pure 1,3,4,5-tetra-acetoxynaphthalene has now been obtained by the reductive acetylation of 3,5-dihydroxy-1,4-naphthoquinone. A mixture of equal amounts of the two pure tetra-acetoxynaphthalenes had the melting point previously reported for the addition product.

The reaction of plumbagin, 2-methyl-5-hydroxy-1,4-naphthoquinone, with acetic anhydride has also been studied. Three products were obtained, but the proportions varied with the conditions. Brief treatment gave principally

plumbagin acetate, but longer reaction times produced the Thiele-Winter addition product, 1,3,4,5-tetra-acetoxy-2-methylnaphthalene, and/or another compound which has not been identified. Hydrolysis of the leucotetra-acetate followed by oxidation gave droserone. Since this work was completed the results of a similar study by Asano and Hase (1943) have become available.

(*c*) *Halogen Derivatives of Juglone and Plumbagin*

It was expected that addition of chlorine or bromine to plumbagin would give a 2,3-dihalide from which 3-chloro- or 3-bromoplumbagin could be obtained by elimination of hydrogen halide. These reactions have long been known to occur with juglone. It was found, however, that the addition of the halogens to plumbagin was slow, and subsequent elimination of hydrogen halide gave mixtures. With excess chlorine in acetic acid, followed by heating with sodium acetate, two products were obtained. One was the expected 2-methyl-3-chloro-5-hydroxy-1,4-naphthoquinone, and the other was presumably 2-methyl-3,6-dichloro-5-hydroxy-1,4-naphthoquinone. As Thomson (1949) has shown that the former can be hydrolysed to droserone, this completes another method for obtaining this pigment from plumbagin. In a similar manner 2-methyl-3-bromo-5-hydroxy-1,4-naphthoquinnoe was also obtained.

When brominated in glacial acetic acid in the presence of anhydrous sodium acetate, juglone gave a monobromo-derivative different from 2- or 3-bromojuglone. This product was evidently 5-hydroxy-6-bromo-1,4-naphthoquinone because it gave 2,3,6-tribromojuglone on further bromination. Similar results were obtained with plumbagin, and the product was presumably 2-methyl-5-hydroxy-6-bromo-1,4-naphthoquinone. Analogous substitutions with chlorine could not be obtained.

5-Hydroxy-8-chloro-1,4-naphthoquinone, prepared by condensation of *p*-chlorophenol, or *p*-bromophenol, with maleic anhydride in a melt of aluminium chloride and sodium chloride, was different from the product described by Gomez (1935), who used the same method of preparation.

II. Experimental

Melting points are corrected and were observed in Pyrex capillaries. Microanalyses by Dr. W. Zimmermann and assistants.

(*a*) *Reaction of Dimethylamine with Naphthoquinones.*—(i) 5-Methoxy-1,4-naphthoquinone was prepared as described by Thomson, Race, and Rowe (1947) and was allowed to react with excess dimethylamine under the conditions used by Anslow and Raistrick (1939) for a similar reaction. However, better yields were obtained when the reaction mixture contained no alcohol. The crude product was hydrolysed by heating for 30 min. on a water-bath with concentrated hydrochloric acid, and the mixture was then diluted and extracted continuously with ether. The hydroxyquinones were extracted from the ether with 5% aqueous sodium carbonate and then precipitated with hydrochloric acid. Yield 42%. The crude product was a mixture of the two isomers which could not be easily separated. Part of the mixture was therefore demethylated with $NaAlCl_4$ as previously described by Cooke and Segal (1950). The crude orange-red product was sublimed in a vacuum and then acetylated to give 2,5-diacetoxy-1,4-naphthoquinone, m.p. 152 °C., alone or mixed with an authentic specimen. Another portion of the mixture was treated with diacetyl peroxide as described by Cooke and Segal (1950), and from the mixed isomers 2-methyl-3-hydroxy-5-methoxy-1,4-naphthoquinone was readily separated. It had m.p. 171–172 °C., not depressed by an authentic specimen.

(ii) 5-Methyl-1,4-naphthoquinone was prepared from benzoquinone and piperylene by the diene synthesis. The general conditions of Fieser (1948) were used. The initial addition product was not isolated but was rearranged with acidified stannous chloride to give *1,4-dihydroxy-5,8-dihydro-5-methylnaphthalene* which separated from aqueous ethanol in colourless needles, m.p. 147 °C. (Found : C, 74·5 ; H, 6·7%. Calc. for $C_{11}H_{12}O_2$: C, 75·0 ; H, 6·8%).

The two stage oxidation of this product gave a 95% conversion to 5-methyl-1,4-naphthoquinone, yellow needles from aqueous acetone, m.p. 122·5–123 °C. Herzenberg and Ruhemann (1927) reported m.p. 102–103° C. and Veselý *et al.* (1929) gave m.p. 121–122 °C. for products prepared by different methods (Found : C, 76·6 ; H, 4·7%. Calc. for $C_{11}H_8O_2$: C, 76·7 ; H, 4·7%).

The reaction of this product with dimethylamine was studied under the conditions used by Plimpton (1880) for 1,4-naphthoquinone. The resulting product was hydrolysed by heating on a water-bath for 45 min. with a mixture of equal volumes of ethanol and concentrated hydrochloric acid. Most of the alcohol was then evaporated and, after dilution with water, the mixture was extracted continuously with ether. The product was recovered as described above and fractionally crystallized from aqueous ethanol. The major product, evidently *3-hydroxy-5-methyl-1,4-naphthoquinone*, formed yellow needles, changing to prisms, m.p. 175–176 °C. (Found : C, 70·1 ; H, 4·3%. Calc. for $C_{11}H_8O_2$: C, 70·2 ; H, 4·3%). The smaller more soluble fraction, m.p. ~134 °C., appeared to contain some of the isomeric compound.

2-Hydroxy-5-methyl-1,4-naphthoquinone was prepared from 5-methyl-1-tetralone by the general method of Buu-Hoï and Cagniant (1942). The product formed pale yellow needles from aqueous methanol, m.p. 145–146 °C. (Found : C, 69·9 ; H, 4·4%. Calc. for $C_{11}H_8O_2$: C, 70·2 ; H, 4·3%).

(iii) 6-Methyl-1,4-naphthoquinone, prepared from benzoquinone and isoprene by the modified diene synthesis of Fieser (1948), crystallized from aqueous acetone as yellow needles, m.p. 91–92 °C. Bendz (1951) reports m.p. 90–91 °C. (Found : C, 76·9 ; H, 4·7%. Calc. for $C_{11}H_8O_2$: C, 76·7 ; H, 4·7%). This compound was allowed to react with dimethylamine as described for the isomer, and the crude product was hydrolysed to give the hydroxynaphthoquinone in 55% yield. This was mostly 2-hydroxy-6-methyl-1,4-naphthoquinone, golden-yellow leaflets from benzene, m.p. 198 °C. Fieser, Hartwell, and Seligman (1936) reported m.p. 199 °C. (Found : C, 70·3 ; H, 4·3%. Calc. for $C_{11}H_8O_2$: C, 70·2 ; H, 4·3%). The methyl ether had m.p. 166·5–167·5 °C. Fieser, Hartwell, and Seligman reported m.p. 167–167·5 °C. No other pure product could be isolated from the more soluble fractions, but small quantities of the isomer may have been present.

(*b*) *Thiele-Winter Reaction with Juglone and Plumbagin.*—(i) *Juglone.* The reaction was repeated as described by Fieser and Dunn (1937), and after many crystallizations the product melted at 154 °C. after softening from 145 °C. The mixture of hydroxyquinones obtained by alkaline hydrolysis of this product was acetylated, and fractional crystallization from benzene-light petroleum (40–60 °C.) readily gave pure 2,5-diacetoxy-1,4-naphthoquinone, m.p. 152–153 °C., not depressed by mixing with an authentic specimen. Reductive acetylation of this material gave 1,2,4,5-tetra-acetoxynaphthalene, m.p. 174 °C., after softening from 167 °C. If allowed to solidify it then melted sharply at 173–174 °C. (cf. Thomson 1951*a*). *1,3,4,5-Tetra-acetoxynaphthalene* was obtained by reductive acetylation of 3,5-dihydroxy-1,4-naphthoquinone. It formed colourless prisms from ethanol, m.p. 167–168 °C. When mixed with an equal amount of 1,2,4,5-tetra-acetoxynaphthalene the m.p. was 154 °C. after softening from 145 °C.

(ii) *Plumbagin.* The quinone (0·1 g.) was dissolved in acetic anhydride (0·8 ml.) and one drop of concentrated sulphuric acid was added. After 24 days, water was added and the dark precipitate purified by sublimation in a vacuum and crystallization from ethanol. The 1,3,4,5-tetra-acetoxy-2-methylnaphthalene formed colourless prisms, m.p. 175·5–176·5 °C. Asano and Hase (1943) reported m.p. 174 °C. (Found : C, 60·7 ; H, 4·9%. Calc. for $C_{19}H_{18}O_8$: C, 61·0 ; H, 4·8%). On hydrolysis with cold methanolic potassium hydroxide, followed by dilution with water and acidification, droserone, m.p. 180–181 °C., was obtained.

When the reaction of acetic anhydride with plumbagin was allowed to proceed for shorter times two other products were obtained in addition to, or instead of, that described above. These products could be separated by fractional sublimation in a vacuum. The more volatile compound

formed large yellow plates from ethanol, m.p. 117–118 °C., and was evidently plumbagin acetate. It could be obtained almost exclusively by reaction at 0 °C. in the presence of only a trace of sulphuric acid, for a time just sufficient to change the colour to yellow. It was never obtained pure under the conditions of Fieser and Dunn (1936), which gave mostly the substance found in the less volatile fraction. This *compound* was sparingly soluble in most solvents, but it crystallized from methyl cellosolve in small colourless needles, m.p. 281–283 °C., uncorr. On standing it rapidly became greenish (Found: C, 67·5; H, 4·4%). This product has not been examined further.

(c) *Halogen Derivatives of Juglone and Plumbagin.*—(i) *5-Hydroxy-6-bromo-1,4-naphthoquinone.* Juglone (0·3 g.) was dissolved in glacial acetic acid (2 ml.) and anhydrous sodium acetate (0·4 g.) was added and well mixed to dissolve as much as possible. A solution of bromine (0·27 g.) in acetic acid (3 ml.) was then added. The flask was stoppered and allowed to stand for 8 days. The precipitated *bromojuglone* was then collected and purified by sublimation in a vacuum and crystallization from light petroleum (90–100 °C.). It formed fine deep orange needles, m.p. 153–154 °C. (Found: C, 47·6; H, 2·2; Br, 31·9%. Calc. for $C_{10}H_5O_3Br$: C, 47·5; H, 2·0; Br, 31·6%).

The *acetyl derivative* formed yellow blades or plates from benzene-light petroleum, m.p. 184–185 °C. (Found: C, 48·6; H, 2·5; Br, 27·8%. Calc. for $C_{12}H_7O_4Br$: C, 48·8; H, 2·4; Br, 27·1%).

(ii) *2,3,6-Tribromojuglone.* The 5-hydroxy-6-bromo-1,4-naphthoquinone (80 mg.) was dissolved in acetic acid (1 ml.) and bromine (0·1 ml.) was added. The mixture was heated for 3 hr. on the water-bath and then cooled. The solid was collected and crystallized from chloroform-light petroleum giving red needles, m.p. 173–175 °C. Thomson (1948) reported m.p. 172 °C. The acetyl derivative formed yellow needles from ethanol, m.p. 188–189 °C. Thomson reported m.p. 188 °C.

(iii) *5-Hydroxy-8-chloro-1,4-naphthoquinone.* Maleic anhydride was condensed with *p*-chlorophenol or *p*-bromophenol as described by Gomez (1935). The product was purified by extraction with light petroleum and, after recovery, by sublimation in a vacuum and finally crystallization from chloroform-light petroleum giving red needles, m.p. 201–202 °C. Gomez reported m.p. 122 °C. (Found: C, 57·2; H, 2·6%. Calc. for $C_{10}H_5O_3Cl$: C, 57·6; H, 2·4%). The acetyl derivative separated from ethanol or benzene-light petroleum in pale yellow needles, m.p. 147–148 °C. Gomez reported m.p. 164 °C. (Found: C, 57·1; H, 2·8; Cl, 14·6%. Calc. for $C_{12}H_7O_4Cl$: C, 57·5; H, 2·8; Cl, 14·2%).

(iv) *2-Methyl-5-hydroxy-6-bromo-1,4-naphthoquinone.* Plumbagin was brominated as described for juglone. The *product* was precipitated with water and purified by sublimation in a vacuum and crystallization from ethanol. It formed deep orange needles, m.p. 183–185 °C. (Found: C, 49·3; H, 2·9; Br, 30·5%. Calc. for $C_{11}H_7O_3Br$: C, 49·5; H, 2·6; Br, 29·9%).

The *acetyl derivative* separated from benzene-light petroleum as yellow prisms, m.p. 135–136 °C. (Found: C, 50·8; H, 3·0; Br, 25·6%. Calc. for $C_{13}H_9O_4Br$: C, 50·5; H, 2·9; Br, 25·8%).

(v) *2-Methyl-3-bromo-5-hydroxy-1,4-naphthoquinone.* The addition of bromine to plumbagin was carried out as described by Thomson (1948) for juglone. The colour faded only slowly over a period of 4 hr., and after boiling the product with ethanol only a small amount of the required product, m.p. 117–118 °C., was isolated. Thomson (1951*b*) reported m.p. 118 °C. for this compound prepared by another method.

(vi) *2-Methyl-3-chloro-5-hydroxy-1,4-naphthoquinone and 2-Methyl-3,6-dichloro-5-hydroxy-1,4-naphthoquinone.* Plumbagin was allowed to react with excess chlorine in acetic acid for 3 hr. The remaining chlorine was then removed by aeration and the mixture was boiled with excess anhydrous sodium acetate. Fractional crystallization of the product from light petroleum gave a less-soluble fraction, the *dichloro-derivative*, which separated in orange-red needles, m.p. 150–151 °C. (Found: C, 51·6; H, 2·6; Cl, 27·6%. Calc. for $C_{11}H_6O_3Cl_2$: C, 51·4; H, 2·3; Cl, 27·6%). The more soluble fraction was finally crystallized from aqueous acetic acid, giving 2-methyl-3-chloro-5-hydroxy-1,4-naphthoquinone as orange-yellow plates, m.p. 123–124 °C Thomson (1949) prepared this compound by another method and reported m.p. 125 °C.

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STUDIES ON THE LIGNIN OF *EUCALYPTUS REGNANS* F. MUELL.

V. ETHANOL LIGNIN

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Summary

Lignin has been isolated from *Eucalyptus regnans* F. Muell. by refluxing with ethanolic hydrogen chloride, and the product separated into an ether-insoluble ethanol lignin-A and an ether-soluble ethanol lignin-B. Ethanol lignin-A has an equivalent weight of 1400 and, on the assumption that the molecular weight is of this order, contains two ethoxyl and nine methoxyl groups. Acetic anhydride and benzoyl chloride in pyridine yield respectively a hepta-acetate and heptabenzoate, while benzoyl chloride in aqueous alkali yields a pentabenzoate. Diazomethane yields a dimethyl derivative which gives a penta-acetate on acetylation. Schotten-Baumann benzoylation of this dimethyl derivative yields a dibenzoate. Two carbonyl groups are present, as shown by the formation of a bisphenylhydrazone and a bis-*p*-nitrophenylhydrazone. The data are consistent with the formula $C_{59}H_{86}O_{16}(OC_2H_5)_2(OCH_3)_9(OH)_7$.

I. INTRODUCTION

The work described in this paper is part of a long-term investigation which has as its object the elucidation of the chemical changes undergone by the lignin of *Eucalyptus regnans* F. Muell. during alkaline pulping. Previous papers in this series have been concerned with the composition of thiolignin and alkali lignins, obtained as by-products from the sulphate and soda pulping of this wood. Ideally, the next step would be the examination of the original lignin, but it is well known that it is only possible to isolate lignin by subjecting the wood to such chemical treatment that it probably undergoes chemical change during isolation. The view is indeed held by many investigators that the lignin does not exist free in wood but is chemically linked to some carbohydrate fraction. It is true that Brauns has shown (1939) that a fraction of the lignin, designated native lignin, may be removed by inert solvent extraction at room temperature, but this amounts to only a small part of the total lignin present. Furthermore, it has recently been shown that this native lignin is identical with the lignin obtained by the enzymatic decomposition of wood (Schubert and Nord 1950), and thus is not above the suspicion of having undergone chemical changes.

It was decided that, although by no means ideal, a method of obtaining information bearing on this subject was to isolate lignin directly from wood by means of one of the standard methods of lignin isolation, and apply the same reaction to isolated alkali lignin. Consideration of all the methods known for this purpose led to the choice of the alcoholysis reaction, that is, the treatment

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of finely divided wood meal with an excess of alcohol in the presence of a catalyst. It is known to give a good yield of a product which is soluble in organic solvents, and has been widely studied over a range of different hydroxy compounds. It is also known that the alcohol used functions not only as a solvent, but reacts with the lignin, the product containing introduced alkoxyl groups. These can be removed by acid hydrolysis (Hägglund, Johnson, and Trygg 1930; Brauns 1939; Charbonnier 1942), and it has been suggested that the reaction involves the formation of an acetal between the alcohol and a carbonyl group in the lignin (Hägglund and Urban 1927; Hägglund, Johnson, and Trygg 1930).

In selecting a suitable alcohol for the purpose consideration was given to benzyl alcohol. Freudenberg and Sohns (1933) recommended it as being very suitable, it is known (Friedman and McCully 1938) to give almost a theoretical yield of isolated lignin, and it has the advantage that benzyl iodide does not interfere in the determination of methoxyl. However it was found that the product contained carbohydrate from which it could not be freed. *cyclo*Hexanol was investigated briefly, and was found to react rapidly and give a good yield of isolated lignin, but the low methoxyl content (13·8 per cent.) indicated either considerable substitution of *cyclo*hexyl units or demethylation. Dioxan was investigated briefly and found unsatisfactory.

Of the lower aliphatic alcohols, it was considered unwise to use methanol for the isolation of a methoxylated product, as it would not be possible to distinguish between the methoxyl groups originally present and those introduced by alcoholysis. Of the other alcohols by far the most widely investigated has been ethanol, and it was decided to select this as the most suitable reagent. It has been found (Patterson *et al.* 1941) that 64–71 per cent. of the total lignin of maple may be recovered as ethanol-soluble ethanol lignin, and that the reaction is accompanied by a depolymerization to low boiling water-soluble compounds and a polymerization to ethanol-insoluble products. These workers also found that the ethanol lignin may be separated into water-soluble, ether-soluble, and ether-insoluble fractions, while Lovell and Hibbert (1941) found these fractions could be further separated by a solvent fractionation technique.

The ethanolysis of maple has been very thoroughly studied by Hewson, McCarthy, and Hibbert (1941) both at the boiling point and under pressure, and from consideration of their findings, the technique of Patterson and co-workers, namely, 48 hr. refluxing with 2 per cent. anhydrous hydrogen chloride as catalyst, was employed. Two series of ethanolyses were carried out, in the presence and absence of air, and the present paper is concerned with the ethanolysis of *E. regnans* in the presence of air.

When *E. regnans* wood meal was refluxed with 2 per cent. ethanolic hydrogen chloride for 48 hr., a yield of crude ethanol-soluble ethanol lignin was obtained equal to 86 per cent. of the original lignin content. This contained a trace (0·62 per cent.) of xylan. After two purifications from acetone-water the yield dropped to 72 per cent. of the original lignin, and the xylan content to less than 0·2 per cent.

Using the technique of Hibbert and co-workers (Patterson *et al.* 1941) for separation into ether-soluble and -insoluble fractions, namely precipitation

of a 10 per cent. solution in acetone with 20 volumes of ether, the water-insoluble ethanol lignin from *E. regnans* was separated into equal amounts of ether-soluble and -insoluble fractions. But this method of separation was found unsatisfactory in that the ether-soluble fraction was not homogeneous, and on refractionating it under these conditions a further yield of ether-insoluble material was found. Finally, the method used previously for *E. regnans* lignins, precipitation of a 10 per cent. solution in dioxan with 10 volumes of ether, was found more satisfactory. After five such separations *E. regnans* ethanol lignin yielded 49·2 per cent. ether-insoluble ethanol lignin-A and 11·4 per cent. of ether-soluble ethanol lignin-B. The former was brown in colour, and started to soften and decompose at 198 °C. The latter was light tan with a decomposition point of 127–130 °C. In addition there was obtained 25·8 per cent. of an intermediate fraction which could be separated by further purification.

The analysis of these lignins for ethoxyl presented some difficulty. Phillips and Goss (1937) claimed to have obtained reliable values for ethoxyl and methoxyl by a modification of the original method of Willstätter and Utzinger, whereby the mixed iodides from a Zeisel hydrolysis are absorbed in trimethylamine, but Cooke and Hibbert (1943) stated that it is difficult to isolate the ethyl iodide quantitatively. Using the technique of Phillips and Goss in this Laboratory on a sample of 3-methoxy-4-ethoxybenzoic acid as standard, the following results were obtained:

OCH_3 15·6, 15·8, 15·4, 15·5, 15·8, 15·6 (calc. 15·8%)
OC_2H_5 18·7, 19·2, 17·3, 19·8, 19·1, 20·8 (calc. 23·0%)

thus confirming the remarks of Cooke and Hibbert. Various attempts were made to improve on this but it was found impossible to obtain reliable values for ethoxyl, and it became necessary to devise some other method. The choice lay between determining ethoxyl directly, for example, by the method of Lemieux and Purves (1947) using a C-methyl determination, and determining total alkoxyl as suggested by Cooke and Hibbert.

When 3-methoxy-4-ethoxybenzoic acid was analysed by the method of Viebock and Brecker (1930) the total alkoxyl content, expressed as methoxyl, was found to be in excellent agreement with the calculated value, and it was decided as a result to analyse ethanol lignin fractions both for total alkoxyl by this method and for methoxyl by the method of Willstätter and Utzinger.

The alkoxyl content of *E. regnans* ethanol lignin-A was found to be 24·6 per cent. as methoxyl, of which 20·0 per cent. was methoxyl. Hence the ratio of methoxyl to ethoxyl groups is 4·3 to 1. Now by potentiometric titration the equivalent weight was found to be of the order of magnitude of 1400, and thus the minimum molecular weight must be of this order. This corresponds to the presence of two ethoxyl groups, and on the basis of 11 total alkoxyl groups the analysis of ethanol lignin-A gave the following empirical formula:

C		62·3%	72·0
H		5·9%	81·3
O		31·8%	27·6
OR		24·6%	*11*
OCH_3	as OCH_3	20·0%	9·0
OC_2H_5		4·6%	2·1

The formula $C_{72}H_{82}O_{28}$ with nine methoxyl and two ethoxyl groups was accordingly adopted as a tentative working hypothesis.

When treated with acetic anhydride in pyridine, ethanol lignin-A yielded an acetate with the following composition (oxygen and ethoxyl by difference):

C	.. .. ..	61·3%	85·7
H	.. .. ..	5·7%	95·0
O	.. .. ..	33·0%	34·6
OR		20·3%	*11*
OCH_3	as OCH_3 ..	16·5%	8·9
OC_2H_5		3·8%	2·0
$COCH_3$	.. ..	18·0%	7·0

Thus we see that the ratio of acetylable hydroxyl to methoxyl groups is seven to nine. Confirmation of this was found by treating ethanol lignin-A with benzoyl chloride in pyridine to yield a heptabenzoate.

In order to obtain some information as to the nature of these hydroxyl groups, the following experiments were carried out. Firstly, ethanol lignin-A was treated with diazomethane in dioxan until no further increase in methoxyl occurred. The analysis of this methylated product, calculated on the basis that no change in oxygen content occurred, was as follows (oxygen and ethoxyl by difference):

C	.. .. ..	62·5%	74·5
H	.. .. ..	6·2%	87·9
O	.. .. ..	31·3%	*28*
OR		28·3%	13·0
OCH_3	as OCH_3 ..	23·8%	11·0
OC_2H_5	.. ..	4·5%	2·1

and indicated that of the seven hydroxyl groups present two are sufficiently acidic to react with diazomethane.

This was confirmed by acetylation of the methylated lignin, whereby the remaining five hydroxyl groups reacted to give a penta-acetate. On the other hand, when the methylated lignin was treated with benzoyl chloride in pyridine, anomalous results were obtained. Although the alkoxyl and methoxyl values agreed well with the values calculated for the expected pentabenzoate, the carbon content was about 1·5 per cent. too low. These values were unchanged by further purification or by repeating the preparation.

Additional data on these five hydroxyl groups were obtained from the Schotten-Baumann reaction. Of the seven hydroxyl groups present in ethanol lignin-A only five react with benzoyl chloride in aqueous alkali, indicating the presence of two hydroxyl groups which are either tertiary alcoholic or in some other manner sterically hindered (cf. Merewether 1948; Freudenberg 1949). It was expected from this that when diazomethane methylated ethanol lignin-A was treated with benzoyl chloride under these conditions, a tribenzoate would result. This was not the case, a dibenzoate being formed. Apparently one of the hydroxyl groups is adjacent to an acidic hydroxyl group, which, when methylated, sterically hinders it from reacting in the Schotten-Baumann reaction. The two hydroxyls which do react when methylated ethanol lignin-A is

TABLE 1

ETHANOL LIGNIN-A FROM THE ETHANOLYSIS OF E. REGNANS IN THE PRESENCE OF AIR

No.	Compound	Empirical Formula	Constituent Groups					C (%)	H (%)	N (%)	OR (%)	OCH_3 (%)	$COCH_3$ (%)
			OC_2H_5	OCH_3	OH	Acyl							
1	Ethanol lignin-A	$C_{72}H_{82}O_{28}=1395$	2	9	7	0	f.	62·3	5·9	—	24·6	20·0	—
							c.	62·1	5·9	—	24·5	20·0	—
2	No. 1+CH_2N_2	$C_{74}H_{86}O_{28}=1423$	2	11	5	0	f.	62·5	6·2	—	28·3	23·8	—
							c.	62·5	6·1	—	28·3	24·0	—
3	No. 1+Ac_2O	$C_{86}H_{96}O_{35}=1690$	2	9	0	7	f.	61·3	5·7	—	20·3	16·5	18·0
							c.	61·3	5·7	—	20·2	16·5	17·8
4	No. 2+Ac_2O	$C_{84}H_{96}O_{33}=1633$	2	11	0	5	f.	62·0	5·8	—	24·6	21·0	13·5
							c.	61·7	5·9	—	24·7	20·9	13·2
5	No. 1+BzCl in C_5H_5N	$C_{121}H_{110}O_{35}=2124$	2	9	0	7	f.	68·4	5·3	—	16·2	13·1	—
							c.	68·4	5·2	—	16·1	13·1	—
6	No. 1+BzCl in NaOH	$C_{107}H_{102}O_{33}=1916$	2	9	2	5	f.	67·0	5·4	—	17·5	15·2	—
							c.	67·1	5·4	—	17·8	14·6	—
7	No. 2+BzCl in C_5H_5N	$C_{109}H_{106}O_{33}=1944$	2	11	0	5	f.	65·8	5·5	—	20·6	17·8	—
							c.	67·3	5·5	—	20·7	17·6	—
8	No. 2+BzCl in NaOH	$C_{88}H_{94}O_{30}=1632$	2	11	3	2	f.	64·8	5·8	—	25·1	20·9	—
							c.	64·7	5·8	—	24·7	20·9	—
9	No. 1+Ph.$NH.NH_2$	$C_{84}H_{94}O_{26}N_4=1576$	2	9	—	—	f.	64·4	6·0	3·5	21·6	17·7	—
							c.	64·1	6·0	3·6	21·7	17·7	—
10	No. 1+p-$NO_2.C_6H_4.NH.NH_2$	$C_{84}H_{92}O_{30}N_6=1666$	2	9	—	—	f.	60·6	5·6	5·1	20·5	16·8	—
							c.	60·6	5·6	5·1	20·5	16·8	—
11	No. 1+m-$NO_2.C_6H_4.CHO$	$C_{79}H_{85}O_{30}N=1529$	2	9	—	—	f.	62·4	5·7	0·9	22·5	18·6	—
							c.	62·2	5·6	0·9	22·3	18·3	—

benzoylated in aqueous alkali are presumably secondary alcoholic in nature. The absence of primary alcoholic hydroxyl groups was shown by the fact that no reaction took place when ethanol lignin-A was treated with triphenylmethyl chloride in pyridine.

Of the two acidic hydroxyl groups at least one is enolic, a positive spot test for enols being obtained. It is possible that both are enolic, as there were found to be two carbonyl groups present. Treatment of ethanol lignin-A with phenylhydrazine in acetic acid yielded a bisphenylhydrazone; a bis-*p*-nitrophenylhydrazone resulted when *p*-nitrophenylhydrazine was used. One active methylene group was found to be present, indicated by the formation of a mono-condensation product with *m*-nitrobenzaldehyde.

These results are summarized in Table 1.

A point of interest to lignin chemists is that ethanol lignin-A and its derivatives are quite stable and may be kept for long periods of time without decomposition. Samples of these derivatives had been kept for 18 months when it became desirable to check some methoxyl values, and it will be seen from Table 2 that no change had taken place.

TABLE 2

METHOXYL CONTENT OF ETHANOL LIGNIN-A DERIVATIVES

Compound	When Made (%)	After 18 Months (%)
Ethanol lignin-A	24·8	24·6
Dimethyl ethanol lignin-A	28·2	28·1
Heptabenzoyl ethanol lignin-A	16·2	16·2
Pentabenzoyl ethanol lignin-A	17·3	17·5
Penta-acetyldimethyl ethanol lignin-A	24·8	24·6
Pentabenzoyldimethyl ethanol lignin-A ..	20·6	20·6

II. EXPERIMENTAL

(*a*) *Preparation of Wood Meal.*—Chips of 21-year old *E. regnans* from Powelltown, Victoria, were ground in a Wiley mill to pass a 40 mesh screen, and the wood meal successively extracted with 1 : 2 ethanol-benzene, ethanol, and water. After each extraction the wood meal was dried at 105 °C., and analysed for Klason lignin, and the methoxyl content of the latter determined. Lignin determinations were also carried out after giving the sample a preliminary extraction with boiling N/8 NaOH for 1 hr., but expressing the results as a percentage of the solvent extracted wood. These data are shown in Table 3.

(*b*) *Ethanolysis of Wood Meal.*—The extracted wood meal (500 g.) was refluxed for 48 hr. with absolute ethanol (3 l.) containing anhydrous hydrogen chloride (60 g. = 2%). The residual wood meal was then filtered off, washed with ethanol until the washings were almost colourless, and dried at 105 °C. Yield 270 g. (54%) (Found: Klason lignin, 10·9; Klason lignin after extraction with N/8 NaOH, 5·7; N/8 NaOH soluble, 19·3; pyridine-soluble, 6·0%).

The combined ethanolic filtrate and washings were concentrated to about 1 l., treated with a solid sodium bicarbonate until the hydrogen chloride was neutralized, filtered, and added dropwise with stirring to distilled water (11 l.). The crude ethanol lignin was filtered off, washed

with water, and dried over H_2SO_4 at 20 mm. Yield 92·0 g. (18·4%) (Found: xylan, 0·62%). This was then purified twice from acetone-water. Yield 77·2 g. (Found: xylan, less than 0·2%).

The ethanol lignin was then dissolved in dioxan to give a 10% solution, filtered, and added dropwise with stirring to 10 volumes of anhydrous ether. The precipitated ethanol lignin-A was further purified by repeating this operation four times. Yield 37·7 g. (Found: C, 62·3; H, 5·9; OCH_3, 20·0; $OCH_3+OC_2H_5$ as OCH_3, 24·6%; equiv. wt. 1410. Calc. for $C_{72}H_{82}O_{28}$(1395): C, 62·1; H, 5·9; OCH_3, 20·0; $OCH_3+OC_2H_5$ as OCH_3, 24·5%). Ethanol lignin-A is a light brown powder softening at 198 °C., is soluble in ethanol, acetone, chloroform acetic acid, ethyl acetate, dioxan, pyridine, and aqueous alkalis, and insoluble in ether, light petroleum, benzene, water, dilute mineral acids, and aqueous sodium bicarbonate.

TABLE 3

EFFECT OF SOLVENT EXTRACTION ON THE LIGNIN CONTENT

No.	Treatment	Soluble (%)	Klason Lignin		Soluble in N/8 NaOH (%)	Klason Lignin after Extraction with N/8 NaOH	
			(%)	OCH_3 in Lignin (%)		(%)	OCH_3 in Lignin (%)
1	None ..		22·0	20·8	16·2	18·4	24·5
2	Extracted with ethanol - benzene	1·2	21·6	20·4	14·9	19·2	22·6
3	No. 2 extracted with ethanol..	0·8	21·3	20·9	14·6	18·6	22·9
4	No. 3 extracted with water ..	6·0	21·4	20·6	16·0	18·9	22·7

The dioxan-ether mother liquors were combined and concentrated to give an approximately 10% solution. This was added dropwise with stirring to 10 volumes of anhydrous ether, precipitating 19·9 g. of a crude intermediate fraction. The mother liquors were now concentrated to give a 5% solution and this time precipitated from 15 volumes of 1 : 1 ether-light petroleum (30–50 °C.), precipitating ethanol lignin-B. Yield 8·8 g. This was purified twice more from chloroform-ether-light petroleum before analysis (Found: C, 61·6; H, 5·7; OCH_3, 20·2; $OCH_3+OC_2H_5$ as OCH_3, 25·0%. Calc. for $C_{71}H_{86}O_{28}$(1381): C, 61·7; H, 5·8; OCH_3, 20·2; $OCH_3+OC_2H_5$ as OCH_3, 24·7%). Ethanol lignin-B is a light tan powder softening at 127 °C. soluble in the same solvents as ethanol lignin-A except that it is slightly soluble in ether and benzene.

(c) *Dimethyl Ethanol Lignin-A.*—Ethanol lignin-A (20 g.) in dioxan (200 cc.) was treated with diazomethane from the alkaline decomposition of nitrosomethylurea (10 g.). It was remethylated twice under the same conditions and isolated from ether. Yield 19·4 g. Yield after two purifications from dioxan ether, 17·8 g. (Found: C, 62·5; H, 6·2; OCH_3, 23·8; $OCH_3+OC_2H_5$ as OCH_3, 28·3%. Calc. for $C_{74}H_{86}O_{28}$(1423): C, 62·5; H, 6·1; OCH_3, 24·0; $OCH_3+OC_2H_5$ as OCH_3, 28·3%). Dimethyl ethanol lignin-A is a light cream coloured powder commencing to soften at 170 °C. It is soluble in acetone, chloroform, dioxan, and pyridine, slightly soluble in acetic acid and ethyl acetate, and insoluble in ethanol, benzene, ether, light petroleum, water, and aqueous alkalis.

(*d*) *Hepta-acetyl Ethanol Lignin-A.*—Ethanol lignin-A (5 g.) in pyridine (25 cc.) was treated with acetic anhydride (15 cc.) for 48 hr. at room temperature. The product was isolated from 1 : 1 ether-light petroleum, and purified once from dioxan-ether-light petroleum and once from chloroform-ether-light petroleum. Yield 4·3 g. (Found : C, 61·3 ; H, 5·7 ; OCH_3, 16·5 ; $OCH_3+OC_2H_5$ as OCH_3, 20·3 ; $COCH_3$, 18·0%. Calc. for $C_{86}H_{96}O_{35}$(1690) : C, 61·3 ; H, 5·7 ; OCH_3, 16·5 ; $OCH_3+OC_2H_5$ as OCH_3, 20·2 ; $COCH_3$, 17·8%).

Hepta-acetyl ethanol lignin-A is a light tan coloured powder with a softening point of 146 °C. It is soluble in the same solvents as ethanol lignin-A except that it is slightly soluble in ether and insoluble in aqueous alkalis.

(*e*) *Penta-acetyldimethyl Ethanol Lignin-A.*—Dimethyl ethanol lignin-A (6·5 g.) in pyridine (35 cc.) was treated with acetic anhydride (25 cc.) for 48 hr. at room temperature. The product was isolated from ether and purified twice from dioxan-ether. Yield 5·7 g. (Found : C, 62·0 ; H, 5·8 ; OCH_3, 21·0 ; $OCH_3+OC_2H_5$ as OCH_3, 24·6 ; $COCH_3$, 13·5%. Calc. for $C_{84}H_{96}O_{33}$(1633) : C, 61·7 ; H, 5·9 ; OCH_3, 20·9 ; $OCH_3+OC_2H_5$ as OCH_3, 24·7 ; $COCH_3$, 13·2%). Penta-acetyldimethyl ethanol lignin-A is a light cream coloured powder with a softening point of 178 °C. It is soluble in acetone, chloroform, acetic acid, ethyl acetate, benzene, dioxan, and pyridine, and insoluble in ethanol, ether, light petroleum, water, and dilute acids and alkalis.

(*f*) *Heptabenzoyl Ethanol Lignin-A.*—Ethanol lignin-A (5 g.) in pyridine (25 cc.) was treated with benzoyl chloride (15 cc.) for 48 hr. at room temperature. The product was isolated from water, and purified from (i) chloroform-ether, (ii) dioxan-water, and (iii) dioxan-ether. Yield (purified) 4·4 g. (Found : C, 68·4 ; H, 5·3 ; OCH_3, 13·1 ; $OCH_3+OC_2H_5$ as OCH_3, 16·2%. Calc. for $C_{121}H_{110}O_{35}$(2124) : C, 68·4 ; H, 5·2 ; OCH_3, 13·1 ; $OCH_3+OC_2H_5$ as OCH_3, 16·1%). Heptabenzoyl ethanol lignin-A is a light brown powder with a softening point of 192 °C. It is soluble in the same solvents as penta-acetyldimethyl ethanol lignin-A except that it is only slightly soluble in acetic acid.

(*g*) *Pentabenzoyl Ethanol Lignin-A.*—Ethanol lignin-A (5 g.) in 10% aqueous sodium hydroxide (50 cc.) was treated with benzoyl chloride (10 cc.). It was purified once from dioxan-water and three times from dioxan-ether. Yield 4·3 g. (Found : C, 67·0 ; H, 5·4 ; OCH_3, 15·2 ; $OCH_3+OC_2H_5$ as OCH_3, 17·5%. Calc. for $C_{107}H_{102}O_{33}$(1916) : C, 67·1 ; H, 5·4 ; OCH_3, 14·6 ; $OCH_3+OC_2H_5$ as OCH_3, 17·8%). Pentabenzoyl ethanol lignin-A is a light brown powder with a softening point of 216 °C., and is soluble in the same solvents as heptabenzoyl ethanol lignin-A.

(*h*) *Pentabenzoyldimethyl Ethanol Lignin-A.*—Dimethyl ethanol lignin-A (3 g.) in pyridine (30 cc.) was treated with benzoyl chloride (10 cc.) for 60 hr. at room temperature. After isolation from water and purification from (i) chloroform-light petroleum, (ii) dioxan-water, and (iii) dioxan-ether, yield 3·0 g. (Found : C, 65·8 ; H, 5·5 ; OCH_3, 17·8 ; $OCH_3+OC_2H_5$ as OCH_3, 20·6%. Calc. for $C_{109}H_{106}O_{33}$(1944) : C, 67·3 ; H, 5·5 ; OCH_3, 17·6 ; $OCH_3+OC_2H_5$ as OCH_3, 20·7%). No significant change in these values was obtained when (i) the product was purified twice more from dioxan-ether, (ii) the experiment was repeated, or (iii) the analysis was carried out by an independent analyst. Pentabenzoyldimethyl ethanol lignin-A is a light brown powder softening at 160 °C. It is soluble in the same solvents as heptabenzoyl ethanol lignin-A except that it is only slightly soluble in ethyl acetate.

(*i*) *Dibenzoyldimethyl Ethanol Lignin-A.*—Dimethyl ethanol lignin-A (3 g.) was suspended in 10% aqueous sodium hydroxide (30 cc.) and benzoyl chloride (10 cc.) added gradually with shaking. The product was purified from (i) chloroform-ether, (ii) dioxan-water, and (iii) dioxan-ether. Yield 2·2 g. (Found : C, 64·8 ; H, 5·8 ; OCH_3, 20·9 ; $OCH_3+OC_2H_5$ as OCH_3, 25·1%. Calc. for $C_{88}H_{94}O_{30}$(1632) : C, 64·7 ; H, 5·8 ; OCH_3, 20·9 ; $OCH_3+OC_2H_5$ as OCH_3, 24·7%). Dibenzoyldimethyl ethanol lignin-A is a dull cream powder softening at 192 °C. and soluble in the same solvents as tetra-acetyldimethyl ethanol lignin-A except that it is only slightly soluble in benzene.

(*j*) *Ethanol Lignin-A Bisphenylhydrazone.*—Ethanol lignin-A (5 g.) in glacial acetic acid (100 cc.) was treated with phenylhydrazine (10 cc.) for 24 hr. on the water-bath. The product was isolated from ether, extracted with ether for 7 hr. in a Soxhlet extractor, and purified twice from dioxan-ether. Yield 4·1 g. (Found : C, 64·4 ; H, 6·0 ; N, 3·5 ; OCH_3, 17·7 ;

$OCH_3+OC_2H_5$ as OCH_3, 21·6%. Calc. for $C_{84}H_{94}N_4O_{26}$(1576): C, 64·1; H, 6·0; N, 3·6; OCH_3, 17·7; $OCH_3+OC_2H_5$ as OCH_3, 21·7%). Ethanol lignin-A bisphenylhydrazone is a brown powder softening at 224 °C. and soluble in the same solvents as ethanol lignin-A except that it is only slightly soluble in ethanol.

(*k*) *Ethanol Lignin-A Bis-*p*-nitrophenylhydrazone.*—Ethanol lignin-A (5 g.) in glacial acetic acid (100 cc.) was treated with *p*-nitrophenylhydrazine (6 g.) for 24 hr. on the water-bath. The product was isolated from ether, extracted with ether for 6 hr. in a Soxhlet extractor, purified twice from dioxan-ether, extracted with ether for a further 6 hr., and purified once more from dioxan-ether. Yield 4·6 g. (Found: C, 60·6; H, 5·6; N, 5·1; OCH_3, 16·8; $OCH_3+OC_2H_5$ as OCH_3, 20·5%. Calc. for $C_{84}H_{92}N_6O_{30}$(1666): C, 60·6; H, 5·6; N, 5·1; OCH_3, 16·8; $OCH_3+OC_2H_5$ as OCH_3, 20·5%). Ethanol lignin-A bis-*p*-nitrophenylhydrazone is a brown powder softening at 218 °C. and soluble in the same solvents as ethanol lignin-A.

(*l*) m-*Nitrobenzal Ethanol Lignin-A.*—Ethanol lignin-A (4 g.) in 10% aqueous sodium hydroxide (40 cc.) was treated with *m*-nitrobenzaldehyde (2·5 g.) for 24 hr. on the water-bath. The product was purified once from dioxan-water, twice from dioxan-ether, extracted with ether for 12 hr., and finally, purified once more from dioxan-ether. Yield 3·1 g. (Found: C, 62·4; H, 5·7; N, 0·9; OCH_3, 18·6; $OCH_3+OC_2H_5$ as OCH_3, 22·5%. Calc. for $C_{79}H_{85}NO_{30}$(1529): C, 62·2; H, 5·6; N, 0·9; OCH_3, 18·3; $OCH_3+OC_2H_5$ as OCH_3, 22·3%). *m*-Nitrobenzal ethanol lignin-A is a brown powder softening at 224 °C. and soluble in the same solvents as ethanol lignin-A except that it is only slightly soluble in ethanol and chloroform.

(*m*) *Attempted Tritylation of Ethanol Lignin-A.*—Ethanol lignin-A (2 g.) in pyridine (20 cc.) was treated with triphenylchloromethane (4 g.) for 48 hr. at room temperature, after which the mixture was poured onto crushed ice. The tarry residue was dissolved on chloroform (50 cc.), the solution washed with water, and then concentrated down to 20–25 cc. The product was isolated from ether and purified twice from dioxan-ether. Yield 1·9 g. (Found: C, 62·6; H, 5·9%. Calc. for ethanol lignin-A: C, 62·3; H, 5·8%).

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COLOURING MATTERS OF AUSTRALIAN PLANTS

III. SYNTHESIS OF 7-METHYLJUGLONE AND RELATED COMPOUNDS

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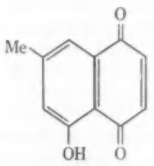
Summary

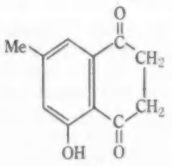
The structures previously assigned to two constituents of *Diospyros hebecarpa* A. Cunn. are confirmed by the synthesis of 5-hydroxy-7-methyl-1,4-naphthoquinone and its conversion to 1,4-diketo-5-hydroxy-7-methyl-1,2,3,4-tetrahydronaphthalene. By an independent route 5-methoxy-7-methyl-1,4-naphthoquinone has also been prepared, and has been converted to 1,4,5-trimethoxy-7-methylnaphthalene.

I. Introduction

In Part II of this series (Cooke and Dowd 1952) the isolation of two new compounds from *Diospyros hebecarpa* A. Cunn. was described. Evidence was presented to show that these compounds must be 5-hydroxy-7-methyl-1,4-naphthoquinone (I) and 1,4-diketo-5-hydroxy-7-methyl-1,2,3,4,-tetrahydronaphthalene (II). The orientation of the substituents was shown by a synthesis of 1,4,5-trimethoxy-7-methylnaphthalene, which did not depress the melting point of the trimethyl ether obtained from II. More conclusive proof of the assigned structures has now been obtained by synthesis of the two natural products.



(I)



(II)

In the first method which was investigated *m*-cresol was succinoylated to the known β-2-hydroxy-4-methylbenzoylpropionic acid. Reduction gave γ-2-hydroxy-4-methylphenylbutyric acid, which was methylated to γ-2-methoxy-4-methylphenylbutyric acid. Oxidation of this product gave methoxyterephthalic acid, confirming the structures assigned to all these compounds. Cyclization with phosphorus oxychloride gave 5-methoxy-7-methyltetralone-1, the oxime of which was converted by the Schroeter reaction to the corresponding naphthylamine. Oxidation of this base with chromic acid gave 5-methoxy-7-methyl-1,4-naphthoquinone. Attempts to demethylate this compound gave

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only very small amounts of hydroxyquinone, which could not be readily purified. This route to the natural products was therefore abandoned. However, the quinone was reduced and methylated to give 1,4,5-trimethoxy-7-methylnaphthalene, previously prepared by a different method, and shown to be identical with the trimethyl ether of II.

The required compounds were finally obtained very readily by the following route. Condensation of maleic anhydride and *p*-chloro-*m*-cresol gave 5-hydroxy-7-methyl-8-chloro-1,4-naphthoquinone. Reductive acetylation followed by hydrogenolysis produced 1,4,5-triacetoxy-7-methylnaphthalene identical with the compound obtained from the natural products I and II. Hydrolysis and oxidation gave 5-hydroxy-7-methyl-1,4-naphthoquinone identical with the natural product I.

The general method of Madinaveitia and Olay (1933) for the preparation of β-hydronaphthoquinones was then applied to the synthetic I. It was reduced to the quinol, which was then fused in a vacuum to isomerize it to 1,4-diketo-5-hydroxy-7-methyl-1,2,3,4-tetrahydronaphthalene, which proved to be identical with the natural product II. It gave no depression of melting point and showed the same ultraviolet absorption spectrum.

II. Experimental

All melting points are corrected and were observed in Pyrex capillaries. Light petroleum refers to the fraction of b.p. 40–60 °C. Microanalyses by Dr. W. Zimmermann and assistants.

(*a*) *Synthesis of 5-Methoxy-7-methyl-1,4-naphthoquinone.*—(i) *β-2-Hydroxy-4-methylbenzoylpropionic Acid.* This preparation is based on the method of Raval, Bokil, and Nargund (1938). Freshly distilled *m*-cresol (50 g.) and succinic anhydride (40 g.) were dissolved in dry tetrachlorethane (200 ml.). The mixture was cooled in ice-salt and powdered anhydrous aluminium chloride (125 g.) was added over a period of 90 min. with the temperature about 0 °C., and the whole apparatus protected from atmospheric moisture. The mixture was shaken at intervals to ensure thorough mixing. The flask was then attached to a short air condenser and was heated in the course of 30 min. to a temperature of 130–140 °C., which was then maintained for 2 hr. At first the mixture frothed vigorously and became quite mobile. During this period it was well shaken at intervals until it became too viscous for further mixing. When cold, the product was treated with crushed ice and concentrated hydrochloric acid. The solvent was removed in steam and the remaining green oil soon crystallized. It was filtered while still hot, dissolved in sodium hydroxide, and boiled with charcoal. After filtration the acid was precipitated with hydrochloric acid and crystallized from ethanol, giving short, slightly green needles, m.p. 153–155 °C. Yield 62%. A small sample was recrystallized several times from ethanol, giving colourless needles, m.p. 155–156 °C. Raval, Bokil, and Nargund (1938) recorded m.p. 154 °C.

From the original aqueous filtrate a small quantity of the *p*-isomer was obtained, m.p. about 170 °C.

(ii) *γ-2-Hydroxy-4-methylphenylbutyric Acid.* The Martin modification of the Clemmensen reduction was applied to the above keto-acid, the mixture being refluxed for 12 hr., with addition of concentrated hydrochloric acid (20 ml.) every 2 hr. After cooling the toluene layer was separated and the aqueous layer was extracted several times with ether. The extracts were added to the toluene, together with a solution of sodium hydroxide (35 g.) in water (300 ml.). The organic solvents were removed by steam distillation and the aqueous solution was acidified while hot with concentrated hydrochloric acid. The precipitated oil crystallized on cooling. A sample for analysis was recrystallized from light petroleum, giving rosettes of fine needles, m.p. 79–80 °C. (Found : C, 68·2 ; H, 7·3%. Calc. for $C_{11}H_{14}O_3$: C, 68·0 ; H, 7·3%).

(iii) *γ-2-Methoxy-4-methylphenylbutyric Acid.* The bulk of the crude acid from the previous step was dissolved in water (400 ml.) with sodium hydroxide (70 g.) and a little sodium dithionite. After heating the solution to 80–90 °C., dimethyl sulphate (75 ml.) was added with vigorous stirring during 20 min. The mixture was then boiled under reflux for 90 min., cooled, washed with ether, and acidified with concentrated hydrochloric acid. The precipitated oil was extracted with ether and dried over sodium sulphate. After evaporation of the ether the oil was distilled under reduced pressure, b.p. 138–140 °C./0·1 mm. A higher boiling fraction was remethylated and recovered in the same way. The total yield of methylated product was then 71% in the two steps from the keto acid. The distilled *acid* crystallized on cooling and a sample was recrystallized from light petroleum, giving wax-like prisms, m.p. 48–50 °C., with previous sintering (Found : C, 69·3 ; H, 7·8 ; OMe, 14·2%. Calc. for $C_{12}H_{16}O_3$: C, 69·2 ; H, 7·8 ; OMe, 14·9%).

The S-*benzylisothiuronium salt* separated from chloroform-light petroleum in long flat prisms, m.p. 125–125·5 °C. (Found : S, 8·4 ; OMe, 8·5%. Calc. for $C_{26}H_{26}O_3N_2S$: S, 8·6 ; OMe, 8·3%).

The structure of the acid was checked by oxidation with excess alkaline permanganate to give methoxyterephthalic acid, which was crystallized from aqueous ethanol in prisms, m.p. 278–279 °C. (uncorr.). Baeyer and Tutein (1889) reported m.p. 276–279 °C. (Found : OMe, 15·9%. Calc. for $C_9H_8O_5$: OMe, 15·8%). Esterification with diazomethane gave the dimethyl ester of methoxyterephthalic acid, which was purified by vacuum sublimation and crystallization from light petroleum to give fine needles, m.p. 71–72 °C. Heilbron—*Dictionary of Organic Compounds*—gives m.p. 71·5 °C. (Found : OMe, 41·2%. Calc. for $C_{11}H_{12}O_5$: 3×OMe, 41·5%).

(iv) *5-Methoxy-7-methyltetralone-1.* A mixture of γ-2-methoxy-4-methylphenylbutyric acid (10 g.) in tetrachlorethane (200 ml.) and phosphorus oxychloride (5 ml.) was heated under an air condenser and drying tube at 130–140 °C. for 2 hr., and then at 160–170 °C. for 30 min. After cooling, the clear solution was decanted from a small amount of tar, and was treated with ice and concentrated hydrochloric acid. The solvent was distilled in steam and the residue was extracted with ether. The ether extract was washed successively with sodium carbonate, sodium hydroxide, and water, and then dried over sodium sulphate. The recovered *product* was distilled, giving a pale yellow-green oil, b.p. 122 °C./0·2 mm. Yield 60%.

The tetralone was converted to the *oxime* by heating with hydroxylamine in aqueous ethanol. The product crystallized from light petroleum (60–80 °C.) in long needles, m.p. 134·5–135 °C. (Found : N, 6·6 ; OMe, 15·1%. Calc. for $C_{12}H_{15}O_2N$: N, 6·8 ; OMe, 15·1%).

(v) *5-Methoxy-7-methyl-1-naphthylamine Hydrochloride.* This preparation was based on the general method of Schroeter (1930). The tetralone oxime (5 g.) was dissolved in purified glacial acetic acid (23 ml.) and acetic anhydride (3 ml.). This solution, protected from atmospheric moisture, was saturated with dry hydrogen chloride. The mixture was then heated on the water-bath for 3 hr., when crystals gradually separated. The mixture was allowed to stand overnight and the *naphthylamine hydrochloride* was filtered, washed with ether, and dried. Yield 54%. A sample was crystallized from hot dilute hydrochloric acid containing a little stannous chloride, and it separated as fine, almost colourless needles, m.p. 250–251 °C. (decomp.) (Found : C, 64·6 ; H, 6·1 ; N, 6·3%. Calc. for $C_{12}H_{14}ONCl$: C, 64·4 ; H, 6·3 ; N, 6·3%).

With excess acetic anhydride in the reaction mixture the *acetyl derivative* of the amine was also obtained. It crystallized from ethanol in flat prisms, m.p. 184·5–185·5 °C.

(vi) *5-Methoxy-7-methyl-1,4-naphthoquinone.* The naphthylamine sulphate (0·31 g. ; obtained by adding concentrated sulphuric acid to a solution of the hydrochloride) was dissolved by warming in water (30 ml.) and concentrated sulphuric acid (1 ml.). The solution was cooled rapidly in ice, and stirred vigorously to give a paste of small sulphate crystals. Then, with continuous stirring, a cold solution of sodium dichromate (0·11 g.) in water (5 ml.) was added during 30 min. After standing overnight in a refrigerator the ice-cold mixture was further oxidized with sodium dichromate (0·22 g.) in water (10 ml.), added during 1 hr. After standing 3 hr., the mixture was extracted eight times with purified ether and the extract was dried rapidly over sodium sulphate and evaporated. The red crystalline *quinone* was sublimed in a vacuum and crystallized from acetone, giving deep orange prisms, m.p. 166·5–167·5 °C. Yield 21%

(Found : C, 71·3 ; H, 4·9 ; OMe, 14·9%. Calc. for $C_{12}H_{10}O_3$: C, 71·3 ; H, 5·0 ; OMe, 15·4%. Several attempts to demethylate this compound gave only very small amounts of impure material giving the reactions of a hydroxyquinone.

(vii) Reductive acetylation gave *1,4-diacetoxy-5-methoxy-7-methylnaphthalene*, which formed prisms from benzene-light petroleum, m.p. 117·5–118·5 °C. (Found : OMe, 10·8%. Calc. for $C_{16}H_{16}O_5$: OMe, 10·8%).

(viii) *1,4,5-Trimethoxy-7-methylnaphihalene* was obtained by adding excess sodium hydroxide solution (containing sodium dithionite) to a solution of the above leucoacetate in methanol and dimethyl sulphate. The reaction was completed by heating under reflux. The product was extracted with ether, dried, recovered, and purified by vacuum sublimation and crystallization from light petroleum. It formed colourless needles or plates, m.p. 112–113 °C., not depressed by mixing with the trimethyl ether of the natural product II (Found : C, 72·4 ; H, 6·9%. Calc. for $C_{14}H_{16}O_3$: C, 72·4 ; H, 6·9%).

(*b*) *Synthesis of the Natural Products.*—(i) *5-Hydroxy-7-methyl-8-chloro-1,4-naphthoquinone.* The preparation is based on the discovery of Gomez (1935) that *p*-chlorophenol can be condensed with maleic anhydride. A mixture of 2-chloro-5-hydroxytoluene (B.D.H., 4 g.) and maleic anhydride (8 g.) was added to a melt of anhydrous aluminium chloride (80 g.) with sodium chloride (16 g.) at 180 °C. The temperature rose to 200 °C. and the mixture was then rapidly cooled with stirring to 120 °C. and poured into a mixture of hydrochloric acid and crushed ice. After standing for a few hours the product was filtered, washed, and dried. The *quinone* was then extracted from the solid with light petroleum in a Soxhlet apparatus, recovered, and further purified by vacuum sublimation. Yield 1·45 g. A small sample crystallized from light petroleum (60–70 °C.) in fine orange-red needles which soon changed to small prisms, m.p. 159–161 °C. (after softening at 147 °C.) (Found : C, 59·5 ; H, 3·2%. Calc. for $C_{11}H_7O_3Cl$: C, 59·3 ; H, 3·2%).

The *leucoacetate* was prepared as usual with zinc dust, acetic anhydride, and sodium acetate. It formed small colourless needles from ethanol, m.p. 163–163·5 °C. (Found : C, 58·5 ; H, 4·4%. Calc. for $C_{17}H_{15}O_6Cl$: C, 58·2 ; H, 4·3%).

(ii) *1,4,5-Triacetoxy-7-methylnaphthalene.* The above leucoacetate (0·5 g.), palladium charcoal (20%, 0·3 g.), and glacial acetic acid (20 ml.) were shaken with hydrogen until absorption ceased. The catalyst was removed and the product was precipitated with water. Yield 85%. Recrystallization from ethanol gave colourless plates, m.p. 175·5–176·5 °C., alone or mixed with the triacetate of the natural product II (Found : C, 64·1 ; H, 5·1%. Calc. for $C_{17}H_{16}O_6$: C, 64·5 ; H, 5·1%).

(iii) *5-Hydroxy-7-methyl-1,4-naphthoquinone.* The triacetoxy-7-methylnaphthalene (0·22 g.) was hydrolysed by refluxing in a nitrogen atmosphere with 5% sodium hydroxide (10 ml.) containing sodium dithionite. The mixture was then acidified with dilute hydrochloric acid, cooled, and treated all at once with ferric chloride (2·5 g.) in water (100 ml.) and concentrated hydrochloric acid (1 ml.). The precipitated quinone was filtered, washed, dried, and sublimed in a vacuum. The deep orange product (yield 70%) was crystallized from light petroleum, giving orange-red needles, m.p. 125·5–126·5 °C., alone or mixed with the natural quinone from *D. hebecarpa* (Found : C, 70·2 ; H, 4·3%. Calc. for $C_{11}H_8O_3$: C, 70·2 ; H, 4·3%).

(iv) *1,4-Diketo-5-hydroxy-7-methyl-1,2,3,4-tetrahydronaphthalene.* The general procedure of Madinaveitia and Olay (1933) was used. The quinone (I) was reduced by shaking an ethereal solution with zinc dust and dilute sulphuric acid until colourless. The ether layer was separated, dried with sodium sulphate, and evaporated to small bulk. The addition of light petroleum precipitated the quinol as a light grey powder which gradually darkened when heated, and melted at 132–135 °C. This compound was sealed in an evacuated glass tube, which was then heated in an oil-bath at 170 °C. for 10 min. The tube was opened and the contents repeatedly extracted with boiling light petroleum. The solid recovered from the extract was sublimed in a vacuum and crystallized, first from light petroleum, and then from aqueous ethanol containing a little sodium dithionate. It formed small colourless needles or plates, m.p. 112–113 °C., alone or mixed with the natural product II. Light absorption : $\lambda_{max.}$ mμ 236, 271, 348 ; log $\varepsilon_{max.}$ 4·37, 3·74, 3·73 (Found : C, 69·3 ; H, 5·2%. Calc. for $C_{11}H_{10}O_3$: C, 69·5 ; H, 5·3%).

III. Acknowledgment

We are indebted to the Dafydd Lewis Trust for a scholarship held by one of us (H.D.) during this work.

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ALKALOIDS OF AUSTRALIAN *STRYCHNOS* SPECIES

I. CONSTITUENTS OF S. LUCIDA R.BR. AND S. PSILOSPERMA F. MUELL.

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Summary

From the fruits of *Strychnos lucida* R.Br. were isolated loganin (1·1 per cent.) which appears to be confined to the pulp, strychnine (0·1 per cent.), brucine (1·3 per cent.), and an unresolved glassy alkaloidal mixture (0·5 per cent.). "Lucidine-S" could not be separated. The leaves of *S. psilosperma* F. Muell. contain about 1·1 per cent. total alkaloid from which two new alkaloids, strychnospermine and spermostrychnine, were isolated. Structural formulae for these are suggested on biogenetic grounds. The triterpene alcohol, germanicol, was also isolated from *S. psilosperma* leaves.

I. Introduction

The genus *Strychnos* is represented in Australia by four species, *S. lucida* R.Br., a shrub extending across northern Australia, belongs to the section Tubiflorae of the genus (which also includes *S. nux-vomica*). *S. psilosperma* F. Muell., a sprawling shrub found mainly in central Queensland near the coast, and *S. arborea* A. W. Hill, a small tree whose range extends farther southwards to northern New South Wales, belong to the section Penicillatae. They are very closely related and botanically the distinctions between them are doubtful. *S. bancroftiana* Bail., thought to belong to the section Lanigerae, is a robust vine restricted to the rain-forests of northern Queensland.

Early work on the alkaloids of the fruit of *S. lucida*, which showed that strychnine and brucine were present, has been summarized by Webb (1948). Later Shaw and de la Lande (1948) claimed that the amount of strychnine present was 0·3 per cent. instead of 0·57–0·84 per cent. as previously reported and that the discrepancy was due to a third alkaloid which was not obtained crystalline or analysed but which was named "lucidine-S". Brucine was found to vary within the limits 1·5–2·4 per cent. in fair agreement with a previous report (1·55 per cent.).

In a reinvestigation two batches of material were examined. From the first, consisting of seeds only, strychnine (0·1 per cent.) and brucine (1·3 per cent.) were isolated in pure crystalline form. The mother liquors contained some amorphous alkaloidal material (0·5 per cent.) which still gave a strong brucine test but from which strychnine was absent. All attempts to obtain from it a pure substance or a fraction which did not give a brucine test failed. The second batch which consisted of seeds plus pulp gave similar results as

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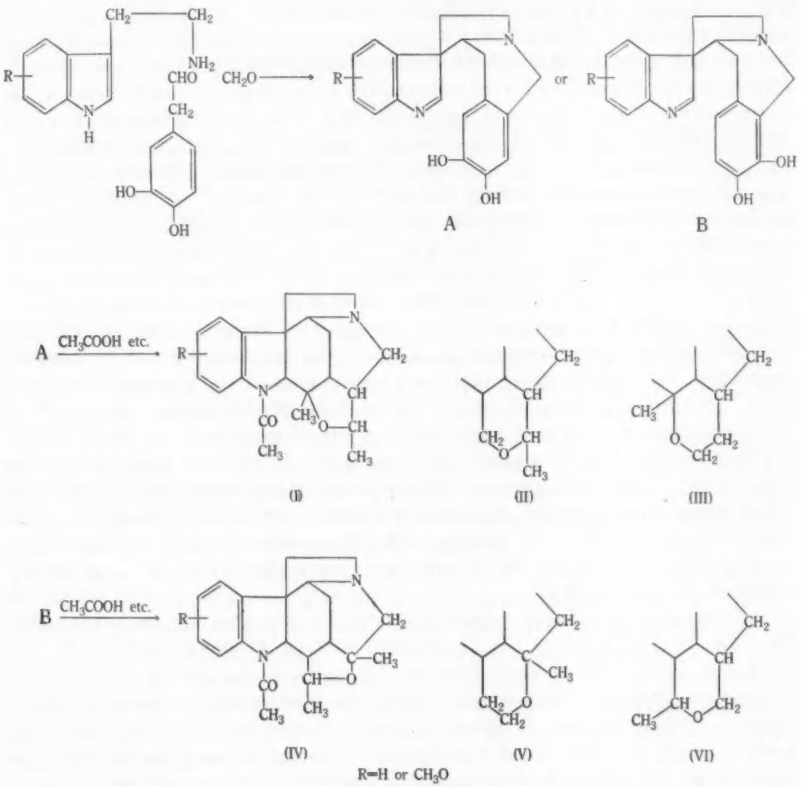
regards alkaloids, but in addition, loganin, the glycoside previously isolated from *S. nux-vomica* pulp (Merz and Krebs 1937) was separated in a yield of 1·1 per cent. These results indicate that loganin occurs only in the pulp. Since Shaw (personal communication) has found that the amount of lucidine-S diminishes with age, the failure to isolate it may be due to the fact that both batches of material were more than a year old when examined.

The leaves of *S. psilosperma* also have been reported to contain strychnine and brucine and in addition strychnicine (Webb 1948). Examination of several samples collected at Dalmar, near Rockhampton, failed to confirm these findings, but two new alkaloids now named strychnospermine (0·9 per cent.) and spermostrychnine (0·05 per cent.) were isolated, the total alkaloid content being about 1·1 per cent. The former was the subject of a brief report (Anet, Hughes, and Ritchie 1950) in which it was assigned the formula $C_{21}H_{28}O_3N_2$ from its analysis and the analyses of its hydrochloride, picrate, methiodide, bromo-derivative, and deacetyl derivative, all of which were in excellent agreement. These substances had been prepared for analysis by drying overnight at 20 mm. at room temperature over sulphuric acid, but it has now been found that this procedure does not give dry samples and that by a remarkable coincidence each of the substances retains sufficient water so that its analysis leads to the above formula. Additional analyses on rigorously dried samples show clearly that the formula should be altered to $C_{22}H_{28}O_3N_2$. It was also stated that the alkaloid contained one methylimino-group since an analysis of the deacetyl derivative gave the value 5·6 per cent. as against the calculated value 9·2 per cent. A re-examination showed that here too an incorrect conclusion had been drawn. Further analyses of the alkaloid and its deacetyl derivative never gave more than 25 per cent. of the calculated values for one methylimino-group, but on the other hand the methiodide analysed for exactly one methylimino-group. The formation of small amounts of alkyl iodide from other alkaloids not containing a methylimino-group in the Herzig-Meyer estimation has been previously recorded (Witkop 1948).

A restatement of the properties of strychnospermine may now be made. The alkaloid, $C_{22}H_{28}O_3N_2$, m.p. 208–209 °C., $[\alpha]_D^{16°}$ +60·3°, contained one methoxyl group but methylenedioxy- and methylimino-groups were absent. Kuhn-Roth determinations showed the presence of at least two and probably three C-methyl groups. It formed a hydrochloride and a picrate and with methyl iodide readily yielded a methiodide showing the presence of a tertiary nitrogen atom. When a small crystal of potassium dichromate was added to its solution in cold concentrated sulphuric acid an intense permanganate colour was immediately produced (positive Otto test). The addition of bromine water to a solution of the alkaloid in dilute acetic acid gave a yellow precipitate which dissolved on shaking and from the reaction mixture bromostrychnospermine was eventually isolated. Strychnospermine could not be hydrogenated in acetic acid with a palladium-charcoal catalyst. Hydrolysis of the alkaloid with either acid or alkali yielded deacetylstrychnospermine, $C_{20}H_{26}O_2N_2$, which was quantitatively reconverted to the parent alkaloid by acetic anhydride. The substance gave a red colour with ferric chloride and an intense blood-red colour

with concentrated nitric acid. It coupled with diazotized sulphanilic acid to form a coloured product similar to methyl orange. None of these reactions is given by strychnospermine, the difference being the same as that between strychnidine or strychninic acid and strychnine. The presence of a secondary nitrogen in the deacetyl derivative was detected by the action of nitrous acid which produced a pale yellow nitroso-derivative, $C_{20}H_{25}O_3N_3$, which gave a



positive Liebermann test. Strychnospermine could not be acetylated or benzoylated nor could derivatives be obtained with ketonic reagents, so the remaining oxygen atom is presumably present in an ether linkage.

The second alkaloid, spermostrychnine, $C_{21}H_{26}O_2N_2$, m.p. 208–209 °C., $[\alpha]_D^{22°}$ +88°, did not contain a methoxyl group but in other respects was similar to strychnospermine, giving the same colour reaction, forming similar derivatives, and possessing the same functional groups. It is therefore thought to be desmethoxystrychnospermine.

The foregoing evidence, although not conclusive, is in accord with the hypothesis that strychnospermine and spermostrychnine are structurally related to the alkaloids of the strychnine group. Woodward (1948) has recently suggested a theory of the biogenesis of these alkaloids and some of his ideas have been applied with conspicuous success by Robinson (1948) to the case of emetine and by Goutarel *et al.* (1950) to the cinchona alkaloids. In the preliminary account of the present work this theory was used to deduce tentative structures for strychnospermine, but in the light of the new evidence, these now require revision (as shown on page 60).

The six alternatives arise from (i) the position in the aldehydic component at which condensation with the formaldehyde equivalent occurs (*A* or *B*), (ii) the manner of closure of the oxide ring, and (iii) the presence of two or three C-methyl groups. If, as seems likely, the condensation leads to *A* as in the case of strychnine itself, and if, as the analytical values appear to indicate, three C-methyl groups are present, then I is the preferred structure.

Two other matters require brief mention. Firstly, some samples of *S. psilosperma* leaves contained a high proportion of deacetylstrychnospermine. This is probably due to enzymatic hydrolysis of the parent alkaloid during drying etc. Secondly, both the leaves and bark of *S. arborea* contain about 0·1 per cent. total alkaloid from which strychnospermine could not be isolated. The distinction between *S. arborea* and *S. psilosperma* therefore appears to be well grounded.

II. Experimental

Analyses are by Miss J. Fildes, University of Sydney, Dr. K. W. Zimmerman, C.S.I.R.O., and Dr. Weiler and Dr. Strauss, Oxford.

(*a*) *Extraction of* S. lucida *Fruit.*—The seeds and pulp, which formed a sticky mass, were soaked for 5 days in absolute alcohol, and then air dried for 2 days. The material was then reasonably tractable and could be milled. The alcohol was used in the subsequent extraction. The ground material (6,000 g.) was moistened with concentrated ammonia (600 cc.) and exhausted with chloroform-alcohol (3 : 1) at room temperature. The extract was evaporated under reduced pressure below 50 °C. as far as possible, the glycoside which crystallized out during the operation being filtered off occasionally. The residue was shaken with water (700 cc.) and chloroform (700 cc.) and the separated layers worked up as follows.

(i) *Aqueous Extract.* After filtration it was evaporated under reduced pressure to a thick syrup which was then taken up in excess absolute alcohol. On concentration more crystalline glycoside separated. This was collected, the filtrate concentrated, excess absolute alcohol added, and the process repeated until no more glycoside was obtained. The total yield of crude, nearly colourless loganin was 68 g. (1·1%). Several recrystallizations from alcohol gave colourless needles, m.p. 214–215 °C. with decomposition (lit. 222–223 °C. corr., with decomp. by rapid heating), $[\alpha]_D^{23°}$ —83° (*c.* 1·102% in water) (lit. $[\alpha]_D^{20°}$ —82·1) (Found: C, 52·1; H, 6·7; CH_3O, 7·8%. Calc. for $C_{17}H_{26}O_{10}$: C, 52·3; H, 6·7; $1\times CH_3O$, 7·9%). The penta-acetyl derivative prepared in nearly quantitative yield by refluxing loganin (3 g.), anhydrous sodium acetate (2·5 g.), and acetic anhydride (25 cc.) for 90 min., crystallized from absolute alcohol in colourless needles, m.p. 141 °C. (lit. 142 °C. corr.) (Found: C, 53·8; H, 6·1; CH_3O, 5·1%. Calc. for $C_{27}H_{36}O_{15}$: C, 54·0; H, 6·0; $1\times CH_3O$, 5·2%).

(ii) *Chloroform Extract.* The residue obtained by evaporation under reduced pressure below 50 °C. was extracted with water (2500 cc.) and concentrated hydrochloric acid (120 cc.) in three portions, the combined extracts were treated with charcoal, filtered, made strongly alkaline with

sodium hydroxide (phenolic bases were absent), and the liberated bases extracted with chloroform. The chloroform was removed and the residue extracted with water (2000 cc.) and concentrated hydrochloric acid (60 cc.) in three portions. The combined acid extracts were then shaken with chloroform (10 × 650 cc.). Evaporation of the chloroform gave a nearly colourless crystalline residue of alkaloid hydrochlorides, fraction 1 (86 g.). The aqueous layer on basification yielded eventually a brown glassy fraction 2 (38 g.).

Fraction 1 was dissolved in water (300 cc.), the solution treated with charcoal, and evaporated under reduced pressure until crystals began to separate. After cooling, these were collected and washed with ice-water (25 cc.) giving nearly pure brucine hydrochloride (43 g.).

The combined filtrates were diluted to 2000 cc., oxalic acid (120 g.) added, followed by concentrated potassium ferrocyanide (15 g.). After 1 hr., the precipitate of strychnine ferrocyanide was collected, washed, and the base regenerated by warming with dilute ammonia. Traces of brucine were removed by stirring with aqueous alcohol (500 cc. of 20%) leaving almost pure strychnine (5·8 g., 0·1%). It crystallized from aqueous alcohol in colourless rhombs, m.p. and mixed m.p. about 270 °C., depending on the rate of heating, and gave the usual colour tests (Found: C, 75·3; H, 6·6; N, 8·4%. Calc. for $C_{21}H_{22}O_2N_2$: C, 75·5; H, 6·6; N, 8·4%). The combined filtrates from the precipitation of strychnine ferrocyanide gave on basification nearly pure brucine (33 g.).

Fraction 2 was dissolved in water (500 cc.) and concentrated hydrochloric acid (20 cc.) giving solution fraction 2S which was shaken with chloroform (150 cc. × 10). Evaporation of the chloroform gave a solid residue (6·4 g.) which was dissolved in water (100 cc.) then treated with a little acetic acid and concentrated aqueous potassium dichromate (8 g.). The crystalline dichromate which separated, on working up gave crude brucine (5 g.). No trace of strychnine could be found in this fraction. The combined brucine fractions (77 g., 1·3%) on recrystallization from benzene gave the anhydrous base as stout opaque needles, m.p. and mixed m.p. 178 °C., which gave the usual colour tests (Found: C, 69·9; H, 6·6; N, 7·2%. Calc. for $C_{23}H_{26}O_4N_2$: C, 70·0; H, 6·6; N, 7·1%).

The aqueous acid liquors fraction 2S contained a brown alkaloidal glass (31 g., 0·5%) from which no crystalline substance could be isolated, nor could any fraction be obtained from it which did not give a strong test for brucine with nitric acid.

Several other procedures for the separation of the alkaloids were tried but the above was found the best. Unless about half of the brucine was first removed the ferrocyanide precipitation of strychnine was unsatisfactory, much brucine being co-precipitated.

In the extraction of seeds without pulp, the preliminary treatment with alcohol was omitted. Loganin was not isolated but otherwise the results were substantially as above.

(*b*) *Extraction of* S. psilosperma *Leaves.*—Extraction with chloroform-alcohol after moistening with ammonia gave the best yield of total alkaloid (1·1%), but the solvent was unsuitable for large amounts of material. The following method was used. The concentrated extract (10 l.) obtained from the dried leaves and branchlets (60 lb.) by continuous hot methanol extraction was worked up in 1 l. batches. After adding 3 volumes of water, the mixture was made acid with concentrated hydrochloric acid (150 cc.), and then chloroform (20 cc.) and alumina (50 g.) were added. The mixture was shaken vigorously and then allowed to stand for 2 days. The liquid was decanted from the viscous black tar which was again extracted with acid (1000 cc. of 1%). The combined acid extract which contained all the alkaloid was shaken with chloroform (3 × 200 cc.) which removed most of the chloroform-soluble impurities as well as a little of the alkaloid. (The residue left after evaporation of the chloroform was extracted with dilute hydrochloric acid and the extract after filtration added to another batch of crude extract.) This aqueous solution was made strongly alkaline with 50% sodium hydroxide and carefully extracted with chloroform (3 × 200 cc.). No difficulty was experienced in this step but the use of ammonia resulted in inseparable emulsions. Evaporation of the chloroform left a yellow crystalline mass which was dissolved in hot dilute hydrochloric acid. Addition of concentrated hydrochloric acid and thorough cooling then readily gave a crystalline product. Further amounts were obtained from the mother liquors by making alkaline, isolating the liberated oil by chloroform extraction, and treating it with acetic anhydride (10 cc.) for 1 hr. at room temperature (to acetylate any

deacetyl bases). The mixture was then taken up in 10% hydrochloric acid and the alkaloid hydrochloride isolated by 12 extractions with chloroform. Total yield 180 g.

Fractional crystallization of the crude product from water ultimately gave pure strychnospermine hydrochloride (150 g.). The bases in the mother liquors were liberated and crystallized several times from acetone to give pure spermostrychnine (10 g.).

From the insoluble residues left after the original acid extractions, germanicol was isolated as follows. The material was refluxed with ethanol (1000 cc.) and potassium hydroxide (100 g.) for 5 hr. and the mixture then concentrated under reduced pressure. The concentrate was extracted with ether, the ether removed, the residue taken up in light petroleum (b.p. 40–60 °C.), and the solution run through a wide column of alumina. Elution with benzene gave a product (20 g.) which was acetylated with acetic anhydride and anhydrous sodium acetate for 2 hr. on the water-bath. The product was crystallized once from boiling ethanol and then chromatographed on alumina from benzene-light petroleum. The middle fractions after crystallization from chloroform-methanol afforded colourless plates, m.p. 269–270 °C., unchanged by further crystallization, $[\alpha]_D^{18°}$ +20° (*c*, 3·0% in chloroform) (Found : C, 81·8 ; H, 11·5%. Calc. for $C_{32}H_{52}O_2$: C, 82·0 ; H, 11·2%). Barton and Brooks (1951) give m.p. 268–270 °C., $[\alpha]_D$ +18° for germanicol acetate.

The free alcohol obtained by alkaline hydrolysis in dioxane-methanol, crystallized from chloroform-methanol, m.p. 173–175 °C., $[\alpha]_D^{16°}$ +5° (*c*, 3·9% in chloroform). The melting point was undepressed by authentic germanicol kindly provided by Dr. D. H. R. Barton who gives m.p. 171–173 °C., $[\alpha]_D$ +4°. The benzoate prepared in pyridine with benzoyl chloride, and crystallized from chloroform-methanol, had m.p. 260–261 °C. (lit. 261–262 °C.). The yield of germanicol was about 1 g., but it was not completely separated from other constituents which were present.

(*c*) *Strychnospermine.*—The *alkaloid* was crystallized from aqueous methanol as colourless needles and dried overnight at 20 mm. at room temperature over concentrated sulphuric acid, m.p. 208–209 °C. (Found : C, 70·6, 70·7, 70·8 ; H, 7·8, 7·9, 7·8 ; N, 7·7, 7·7 ; CH_3O, 8·6, 8·5; CH_3O+NCH_3 as NCH_3, 9·7%. Calc. for $C_{21}H_{25}O_3N_2$: C, 70·9 ; H, 7·9 ; N, 7·9 ; $1\times CH_3O$, 8·7%). After drying at 117 °C. in a pistol it became anhydrous and then had m.p. 208–209 °C., $[\alpha]_D^{16°}$ +60·3±0·5° (*c*, 1·37% in chloroform) (Found : C, 71·5, 71·3, 71·2 ; H, 7·7, 7·4, 7·6 ; N, 7·7 ; C-CH_3, 8·8%. Calc. for $C_{22}H_{28}O_3N_2$: C, 71·7 ; H, 7·7 ; N, 7·6 ; $2\times$C-CH_3, 8·2 ; $3\times$C-CH_3, 12·2%).

The *hydrochloride* crystallized from water in colourless plates which began to char at about 300 °C. and then melted with effervescence at 330–332 °C. It was sparingly soluble in alcohol and cold water but easily soluble in hot water (Found : C, 64·1 ; H, 7·4 ; N, 7·1 ; Cl, 9·0%. Calc. for $C_{21}H_{29}O_3N_2Cl$: C, 64·2 ; H, 7·4 ; N, 7·1 ; Cl, 9·0%). After drying at 117 °C. etc. it had $[\alpha]_D^{15°}$ +66·6±1·0° (*c*, 1·43% in water) (Found : C, 65·0 ; H, 7·5 ; N, 7·1 ; Cl, 8·8%. Calc. for $C_{22}H_{29}O_3N_2Cl$: C, 65·2 ; H, 7·2 ; N, 6·9 ; Cl, 8·8%).

The *picrate* formed yellow needles from alcohol, which began to decompose at about 230 °C., but did not melt until 254 °C. (Found : C, 55·5 ; H, 5·5 ; N, 11·8%. Calc. for $C_{27}H_{31}O_{10}N_5$: C, 55·4 ; H, 5·3 ; N, 12·0%). After drying at 100 °C. etc. it became anhydrous (Found : C, 56·6 ; H, 5·5 ; N, 11·9%. Calc. for $C_{28}H_{31}O_{10}N_5$: C, 56·3 ; H, 5·2 ; N, 11·7%).

The *methiodide* was obtained by adding excess methyl iodide to the powdered base at room temperature. After 1 hr. excess reagent was removed and the residue crystallized from water, forming colourless needles, m.p. 335 °C. (decomp.). The same product was obtained by heating at 100 °C. (Found : C, 53·1 ; H, 6·2 ; N, 5·6%. Calc. for $C_{22}H_{31}O_3N_2I$: C, 53·0 ; H, 6·3 ; N, 5·6%). After crystallizing from methanol-ether and drying at 100 °C. etc. it was obtained anhydrous (Found : C, 53·8 ; H, 6·1 ; N, 5·4 ; CH_3O+NCH_3 as NCH_3, 11·1%. Calc. for $C_{23}H_{31}O_3N_2I$: C, 54·1 ; H, 6·1 ; N, 5·5 ; $1\times CH_3O+1\times NCH_3$ as NCH_3, 11·4%).

(*d*) *Bromostrychnospermine.*—A solution of the alkaloid (3 g.) in dilute acetic acid was shkaen vigorously while saturated bromine water was added. Each drop of reagent caused the formation of a yellow opalescence at first and then later a yellow precipitate which slowly dissolved.

Addition was continued until the precipitate would not redissolve, about 50 cc. being required. After filtering, the *product* was precipitated by ammonia, collected, washed, and recrystallized from aqueous alcohol forming colourless needles (2 g.), m.p. 245 °C. (Found: C, 58·1; H, 6·3; N, 6·4; Br, 18·4%. Calc. for $C_{21}H_{27}O_3N_2Br$: C, 57·9; H, 6·3; N, 6·4; Br, 18·4%). After sublimation at 0·1 mm. it became anhydrous (Found: C, 58·7; H, 6·2; N, 6·5; Br, 18·1%. Calc. for $C_{22}H_{27}O_3N_2Br$: C, 59·1; H, 6·1; N, 6·3; Br, 17·9%).

(*e*) *Deacetylstrychnospermine.*—(i) The *alkaloid* (5 g.) was refluxed for 8 hr. with a solution of potassium hydroxide (10 g.) in water (10 cc.) and alcohol (60 cc.). After removing the solvent, water was added, the *product* collected, and recrystallized from aqueous alcohol, forming colourless flattened needles (4·1 g.), m.p. 222 °C.

(ii) A solution of the alkaloid (3 g.) in concentrated hydrochloric acid (50 cc.) was refluxed for 3 hr. and then evaporated to small bulk. After dilution ammonia was added when the product (1·7 g.) slowly separated. Recrystallization gave colourless flattened needles, m.p. and mixed m.p. 222 °C. (Found: C, 72·8; H, 8·2; N, 8·8; CH_3O, 9·5; NCH_3, 5·6%. Calc. for $C_{19}H_{26}O_2N_2$: C, 72·6; H, 8·3; N, 8·8; $1\times CH_3O$, 9·9; $1\times NCH_3$, 9·2%). After sublimation at 0·1 mm. it became anhydrous (Found: C, 73·9; H, 8·2; N, 8·8; CH_3O+NCH_3 as NCH_3, 12·3; C-CH_3, 5·4%. Calc. for $C_{20}H_{26}O_2N_2$: C, 73·6; H, 8·0; N, 8·6; $1\times CH_3O$ as NCH_3, 8·9; $1\times$C-CH_3, 4·6; $2\times$C-CH_3, 9·2%). The substance was easily soluble in the usual organic solvents. It gave a red colour with ferric chloride, an intense blood-red colour with concentrated nitric acid, and coupled readily with diazonium salts to form red dyes. A negative result was obtained in the Otto test when concentrated sulphuric acid was used, but an intense red colour was formed with 60% sulphuric acid. When treated with acetic anhydride at room temperature the parent alkaloid was quantitatively regenerated.

(*f*) *N-Nitrosodeacetylstrychnospermine.*—A warm solution of deacetylstrychnospermine (1 g., 1 mol.) in water (15 cc.) and concentrated hydrochloric acid (3 cc.) was quickly cooled to 0 °C. and treated rapidly with sodium nitrite (0·23 g., 1 mol.) in water (3 cc.) with stirring below 5 °C. A bright yellow colour was immediately produced and frequently a yellow crystalline precipitate formed but no gas evolved. After stirring for a further 5 min., the mixture was basified with ammonia, and extracted with ether. The extract was washed thoroughly with water, dried, and evaporated. The yellow crystalline residue was difficult to purify because of its high solubility in the usual solvents and its tendency to separate from aqueous methanol or ethanol as an oil. The best specimen obtained formed triangular yellow plates, m.p. 198–199 °C. with decomposition and previous darkening but was evidently not pure (Found: C, 65·8; H, 7·0; N, 12·7%. Calc. for $C_{20}H_{25}O_3N_3$: C, 67·7; H, 7·1; N, 11·8%).

(*g*) *Spermostrychnine.*—The *alkaloid* crystallized from acetone in colourless glistening needles, m.p. 208–209 °C., depressed to about 185 °C. by admixture with strychnospermine. It was readily soluble in cold methanol and gave the same colour reaction as strychnospermine. For analysis it was dried at 100 °C. etc. when it had $[\alpha]_D^{22°}$ +88° (*c*, 2·2% in chloroform) (Found: C, 74·5, 74·6; H, 7·8, 7·9; N, 8·2, 8·0; CH_3O, 0·8; NCH_3, 2·0; C-CH_3, 10·0%. Calc. for $C_{21}H_{26}O_2N_2$: C, 74·6; H, 7·8; N, 8·3; $1\times CH_3O$, 9·2; $1\times NCH_3$, 8·6; $2\times$C-CH_3, 8·9; $3\times$C-CH_3, 13·3%).

The *picrate* crystallized from methanol in small yellow hexagonal plates, m.p. 173–175 °C. (decomp.). It was dried at 100 °C. *in vacuo* (Found: C, 56·4; H, 5·3; N, 11·9%. Calc. for $C_{27}H_{29}O_9N_5.CH_3OH$: C, 56·1; H, 5·6; N, 11·7%).

The *methiodide* crystallized from methanol-ether in glistening needles, m.p. 301–303 °C. Unlike strychnospermine methiodide it was very soluble in water even in the presence of potassium iodide. For analysis it was dried at 100 °C. *in vacuo* (Found: C, 54·9; H, 6·2; N, 6·0; I, 26·2%. Calc. for $C_{22}H_{29}O_2N_2I$: C, 55·0; H, 6·1; N, 5·8; I, 26·4%).

(*h*) *Deacetylspermostrychnine.*—Alkaline hydrolysis was effected as in Section II (*e*). The *product* crystallized from aqueous methanol in colourless needles, m.p. 196–198 °C. For analysis it was sublimed at 150 °C./0·06 mm. when it was obtained as colourless prisms, $[\alpha]_D^{20°}$ −118° (*c*, 2·3% in chloroform) of the same m.p. It gave colour reactions like those of deacetylstrychnospermine (Found: C, 77·0; H, 8·2; N, 9·3; C-CH_3, 7·6%. Calc. for $C_{19}H_{24}O_2N_2$: C, 77·0; H, 8·2; N, 9·5; $1\times$C-CH_3, 5·1; $2\times$C-CH_3, 10·1%).

III. Acknowledgments

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ALKALOIDS OF THE AUSTRALIAN RUTACEAE: *ACRONYCHIA BAUERI* SCHOTT.

IV. ALKALOIDS PRESENT IN THE LEAVES

By J. A. LAMBERTON* and J. R. PRICE†

[*Manuscript received August 4, 1952*]

Summary

The leaves of *Acronychia baueri* Schott. contain the acridine alkaloids melicopine, melicopidine, and melicopicine and the furoquinolines skimmianine, acronycidine, and kokusaginine, the structures of which have all been established previously. In addition two new alkaloids are present. These are 2,4-dimethoxy-10-methylacridone (I) and a dimethoxydimethylpyranofuroquinoline which has been named acronidine. Acronidine has been degraded to a phenol which on methylation gives *iso*kokusaginine (II). The alkaloid must therefore possess structure III or IV, the latter being preferred.

I. ISOLATION OF THE ALKALOIDS

In Part I of this series, dealing with the alkaloids in the bark of *Acronychia baueri* Schott., Lahey and Thomas (1949) also reported a preliminary examination of the basic constituents of the leaves. They identified melicopicine (1,2,3,4-tetramethoxy-10-methylacridone) and indicated that other, more strongly basic, alkaloids are present. Eight alkaloids have now been isolated in a pure condition, six of them having been isolated previously from other sources and their structures established. They are the N-methylacridones melicopicine, melicopidine, and melicopine and the furoquinolines kokusaginine, skimmianine, and acronycidine. Of the two new alkaloids, one has been identified as 2,4-dimethoxy-10-methylacridone, the other is given the name acronidine. Yields and references to structure are listed in Table 1. The values should be regarded only as a general guide to the alkaloid content; the amounts present in the plant are certainly somewhat greater. The separation of the bases was facilitated by the sparing solubility of kokusaginine hydrochloride and by the fact that 2,4-dimethoxy-10-methylacridone separates as a hydrate when a solution in benzene is shaken with water.

2,4-Dimethoxy-10-methylacridone has been identified by comparison of the base and its picrate with specimens synthesized by Drummond and Lahey (1949) and by conversion to 2-methoxy-4-hydroxy-10-methylacridone, which was likewise compared with a synthetic specimen. The ultraviolet absorption spectra of 2,4-dimethoxy- and 2-methoxy-4-hydroxy-10-methylacridone have

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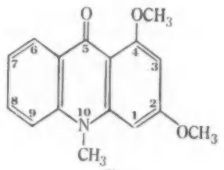
been measured for comparison with the spectrum of the 2,4-dihydroxy- compound reported by Brown and Lahey (1950). In addition, the spectrum of 1-methoxy-

TABLE 1
YIELDS OF PURIFIED ALKALOIDS

Alkaloid	Yield (%)	Reference to Structure
Melicopicine	0·26	Crow and Price (1949)
Melicopidine	0·14	Crow and Price (1949)
Melicopine	0·01	Crow and Price (1949)
2,4-Dimethoxy-10-methyl-acridone	0·05	Present work
Kokusaginine	0·04	Anet, Gilham, Gow, Hughes, and Ritchie (1952)
Skimmianine	0·016	Asahina and Inubuse (1930)
Acronycidine	0·005	Lahey, Lamberton, and Price (1950)
Acronidine	0·06	Present work



(I)

10-methylacridone has been measured in order to complete the series of mono-methoxy-10-methylacridones ; the data are presented in Table 2 and Figure 1. Brown and Lahey state that the intensity of the V_{2f} band* of 10-methylacridone

TABLE 2
ULTRAVIOLET ABSORPTION DATA

Substance	$\lambda_{max.}$ (mμ)	Log $\varepsilon_{max.}$	$\lambda_{max.}$ (mμ)	Log $\varepsilon_{max.}$	$\lambda_{max.}$ (mμ)	Log $\varepsilon_{max.}$
1 - Methoxy - 10 - methyl-acridone	*410*	3·89	312	3·64	262	4·60
	398	3·91	302	3·63		
2,4 - Dimethoxy - 10 - methylacridone	380	3·94	*~315*	3·75	267	4·67
			289·5	4·15	261	4·66
					~250	4·50
2 - Methoxy - 4 - hydroxy-10-methylacridone	390	3·79	322·5	3·81	269·5	4·67
			293	4·08	262	4·63
					~250	4·45

* Brown and Lahey designate the three band systems as the V_1 (longer wavelength), V_{2f} (middle region), and V_{2p} (shorter wavelength) bands respectively.

is increased by introducing a methoxyl substituent. Such an increase (which, in fact, is not shown by their data in the case of the 3-methoxy-compound) is observed for 1-methoxy-10-methylacridone, but it is not as great as for the 2- and 4-methoxy-compounds. Brown and Lahey also point out that the introduction of a methoxyl group in the 2- or 4-positions leads to a shift of the V_1 band to shorter wavelengths, while a methoxyl group in the 3-position causes a shift of this band to longer wavelengths. Comparison of the spectra of 1,2,3,4-tetramethoxy-, 1,2-methylenedioxy-3,4-dimethoxy-, and 2,3-methylenedioxy-1,4-dimethoxy-10-methylacridones led them to predict that an " unhindered " methoxyl group in the 1-position would cause a greater shift than a methoxyl group in any other position, this shift of course being to longer wavelengths.

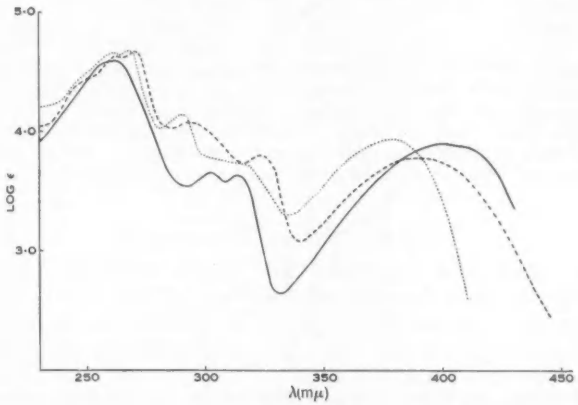


Fig. 1

—— 1-Methoxy-10-Methylacridone.
- - - - 2-Methoxy-4-Hydroxy-10-Methylacridone.
.... 2,4-Dimethoxy-10-Methylacridone.

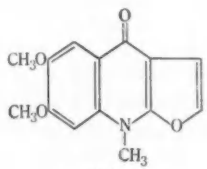
This prediction is not substantiated by measurement ; the V_1 band in 1-methoxy-10-methylacridone *is* located at a longer wavelength than that of 10-methylacridone, but the magnitude of the shift is *less* than for either the 2- or the 3-methoxy-compounds. This discrepancy between prediction and measurement probably arises from the assumption by Brown and Lahey that the methoxyl group in 1-methoxy-10-methylacridone is unhindered, that is, that it can lie in the same plane as the acridone ring. The *peri*N-methyl group may well interfere with this coplanarity and to a greater extent than with a methylenedioxy-substituent. The spectrum of 2,4-dimethoxy-10-methylacridone presents no unexpected features and is very similar to that of acronycinic acid. Demethylation of the 4-methoxyl-group results in a shift of the V_1 band to longer wavelengths, the magnitude of this shift (700 cm.$^{-1}$) being the same as that observed after demethylation of dihydroacronycine.

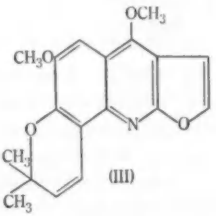
2,4-Dimethoxy-10-methylacridone hydrochloride resembles the hydrochloride of melicopidine (Crow and Price 1949) in that its solubility in aqueous

hydrochloric acid increases with increasing acid concentration. It is of interest that acronycine (Drummond and Lahey 1949), an isoprenoid derivative of 2-hydroxy-4-methoxy-10-methylacridone and the major alkaloidal constituent of the bark of *A. baueri* could not be detected in the leaves.

II. The Structure of Acronidine

Acronidine, $C_{18}H_{17}O_4N$, is a weak base containing two methoxyl groups but no methylimino-group.* It is optically inactive and is insoluble in alkali. Heating with methyl iodide brings about isomerization to *iso*acronidine which contains one methoxyl and one methylimino-group. This isomerization is typical of that observed with the furoquinoline alkaloids (see, for example, Lahey, Lamberton, and Price 1950). Demethylation of one of the methoxyl groups, to give noracronidine, takes place on heating the alkaloid with ethanolic hydrochloric acid. The formation under these conditions of noracronycidine from acronycidine, that is, demethylation of the 4-methoxyl group, has been reported previously and norskimmianine has now been prepared from skimmianine by the same procedure.


(II)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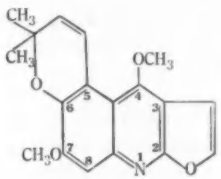

(IV)

The presence of a 2,2-dimethylpyran ring system is implied by the isolation of α-hydroxy*iso*butyric acid after permanganate oxidation. This is in agreement with the result of Kuhn-Roth terminal-methyl group determinations, the *gem*-dimethyl group giving 0·53 mole acetic acid. It is confirmed by the degradation of noracronidine with 30 per cent. potassium hydroxide to a phenol and a mixture of acetone and acetaldehyde which were separated by chromatographing the mixed 2,4-dinitrophenylhydrazones on alumina. Acetone is commonly an alkaline degradation product of 2,2-dimethylpyrano-compounds and its formation excludes the possibility that the α-hydroxy*iso*butyric acid may arise from an *iso*propylfuran ring as it is stated to in the case of oreoselone (see Späth, Klager, and Schlösser 1931).†

* As recorded in Section IV, analyses consistently showed a small positive result in the CH_3N determination, c. 20 per cent. of one CH_3N group. The discrepancy is attributed to formation of some volatile iodide by partial breakdown of the pyran ring. The result of the CH_3N determination on *iso*acronidine, which contains one CH_3N group, was also c. 16 per cent. high.

† α-Hydroxy*iso*butyric acid was stated to be formed when oreoselone is oxidized with alkaline permanganate. Later, Späth and Klager (1933) obtained α-hydroxy*iso*valeric acid by oxidation with acid permanganate and *iso*butyric acid by oxidation with alkaline hydrogen peroxide.

The phenolic product from the action of potassium hydroxide on noracronidine was not isolated as such. The reaction mixture was methylated directly giving in good yield a colourless weakly basic substance $C_{14}H_{13}O_4N$ containing two methoxyl groups and one methylimino-group. This was identified as *iso*kokusaginine (II) by m.p. and mixed m.p., ultraviolet absorption spectrum (Fig. 2) and R_F value for butanol-acetic acid. Its structure has been established by Anet *et al.* (1952). It follows that acronidine must have structure III or IV, that is, either position 5 or 8 is unsubstituted. In a molecule of this kind, coupling with diazonium salts should occur at position 6 or 8;

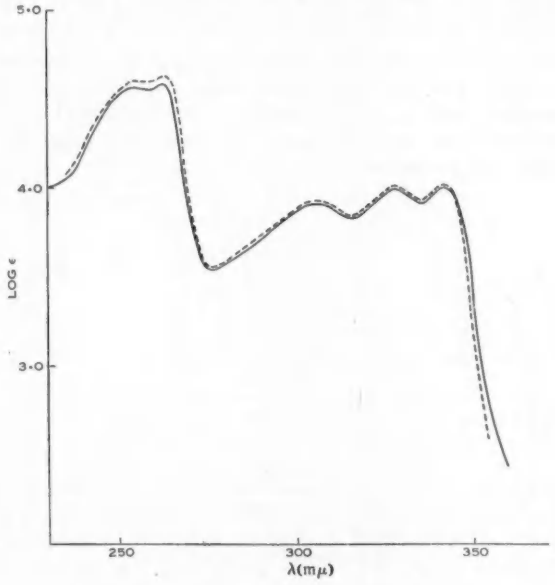


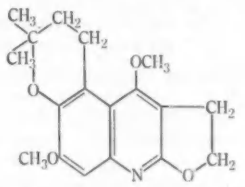
Fig. 2

—— *iso*Kokusaginine from degradation of acronidine.
- - - - *iso*Kokusaginine, authentic.

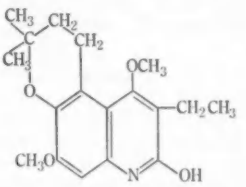
noracronycidine, for instance, with only the 6-position free, couples readily. Noracronidine also couples, and since position 6 is excluded, acronidine evidently possesses structure IV. This conclusion, however, requires confirmation.

Hydrogenation of acronidine over Raney nickel gives a mixture of tetrahydroacronidine (V) and the dihydropyranoquinolone, $C_{18}H_{23}O_4N$ (VI), arising by hydrogenolysis of the furan ring. C-methyl determinations on this substance show 1·85 terminal-methyl groups compared with 0·82 for tetrahydroacronidine. Like carbostyril and unlike tetrahydroacronidine, VI is only sparingly soluble in boiling 1 per cent. hydrochloric acid, but unlike carbostyril it is insoluble in hot aqueous sodium hydroxide. A number of 3-alkylcarbostyrils have been synthesized by Searles and Lindwall (1946) and we are indebted to Dr. A. Langley

Searles, Department of Chemistry, New York University, for the information that these compounds are virtually insoluble in alkali. 3-Ethyl-4-methyl carbostyril, for example, does not give a colour with ferric chloride and is insoluble even in hot 30 per cent. aqueous sodium hydroxide. In agreement with the conclusion of Papa, Schwenk, and Ginsberg (1951) that hydrogenolysis of the furan ring (with Raney nickel and alkali) occurs as a competitive reaction with hydrogenation and must precede hydrogenation, we find tetrahydroacronidine to be unchanged by further treatment with Raney nickel and hydrogen.



(V)



(VI)

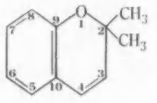
The ultraviolet absorption spectra of acronidine and a number of its derivatives have been measured but will be reported in a later paper.

III. Fission of the Dimethylpyran Ring

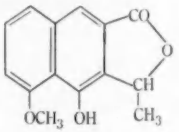
While the formation of acetone by alkaline hydrolysis of noracronidine is in keeping with the behaviour of many 2,2-dimethylpyrans, the co-formation of acetaldehyde is unique. In most other instances all five carbon atoms of the isoprene unit are split off, but only the three represented by the acetone have been identified, and since the conditions of hydrolysis are severe, the fate of carbon atoms 3 and 4 has generally been disregarded. It has been suggested (Wawzonek 1951) that the formation of acetone is good proof for a 2,2-dimethylchromene structure, but it is not a diagnostic test as not all 2,2-dimethylchromenes give acetone under these conditions. 2,2-Dimethylchromene (Shriner and Sharp 1939), 2,2,6-trimethyl-3,4-benzochromene (Cahn 1933), and 2,2-dimethyl-5,7,8-trimethoxy-6-acetylchromene (evodione ; Wright 1948) are not attacked by alkali while the 2,2-dimethylpyranoacridone, acronycine, undergoes ring fission without degradation (Brown *et al.* 1949). On the other hand, from nine coumarins, *iso*flavones, rotenoids, and acetophenones containing the 2,2-dimethylpyran ring, all five carbon atoms are split off, three being recovered as acetone. 2,2-Diphenyl-4-methoxychromene (Heilbron and Hill 1927) behaves likewise giving benzophenone, but replacement of the 4-methoxyl group by methyl leads to a different type of fission, four 2,2-diphenyl-4-methylchromenes (Heilbron and Hill 1927 ; Kartha and Menon 1943) giving benzhydryl phenyl ethers. In the one instance in which a search was made, lactaldehyde was isolated as the second product.

The nine dimethylpyrans which give acetone as the only volatile product all contain a substituent carbonyl or –CH=CH–COOH group in the *p*-position (eight) or an *o*-position (one) to the pyran oxygen atom. The electron-attracting character of these substituent groups renders C_9 (see formula VII) more susceptible to anionic attack and so facilitates opening of the pyran ring by

fission of the C_9–O_1 bond. Following opening of the ring, acetone can split off by a retrograde aldol condensation. Subsequent attack by hydroxyl ion at C_4 would give an intermediate analogous to the naphthalene derivative eleutherol (VIII) from which acetaldehyde is split off almost quantitatively by heating with dilute aqueous potassium hydroxide (Schmid, Meijer, and Ebnöther 1950). Previous workers have isolated and identified the acetone as its 2,4-dinitrophenylhydrazone which usually requires repeated crystallization (see, for

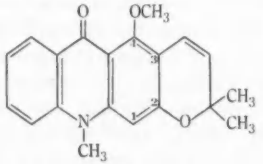


(VII)

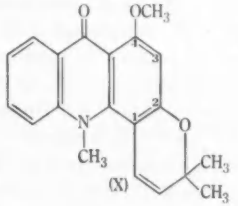


(VIII)

example, Wolfrom *et al.* 1946) so it is possible that in some cases a small amount of acetaldehyde is recovered, but has not been detected. The effective absence of acetaldehyde is probably due to the rate of formation being so low that the aldehyde polymerizes before it can be removed by volatilization. A similar situation exists in the alkaline hydrolysis of coumarins. A number of instances are on record where carbon atoms 2,3, and 4 of the α-pyrone ring are eliminated but no acetaldehyde or other volatile carbonyl compound has been detected. On the other hand, 7-hydroxy-3-phenyl-4-methylcoumarin gives benzyl methyl ketone in good yield, together with resorcinol (Baker 1925).



(IX)



(X)

With the alkaloid acronycine (IX or X) the pyran ring is opened easily as a consequence of activation by the acridone oxygen atom, but the electron availability at C_3 (or C_1; IX or X) evidently does not favour breakdown of the carbinol and degradation proceeds no further. In noracronidine, on the other hand, the isoprene chain is attached at a position of low electron availability and when the pyran ring is opened both retrograde aldol condensations should be facilitated, so that the second can give rise to acetaldehyde sufficiently rapidly to permit volatilization of a substantial proportion before polymerization. The difficulty in the case of noracronidine is concerned with the opening of the pyran ring; nucleophilic substitution at C_6 (formula IV) should be extremely difficult and some other mechanism may be operative. The degradation of 2,2-diphenyl-4-methylchromenes referred to above, which necessarily involves attack by hydroxyl ions at C_3 and C_4, shows the feasibility of ring fission by other than the

" normal " mode of attack at C_9 (formula VII) and it is possible that the O_1–C_2 bond is broken by attack at C_2.* In any event, the formation of acetaldehyde as well as acetone cannot cast doubt on the presence of a 2,2-dimethylpyran ring in acronidine. With regard to the resistance to alkali of 2,2-dimethyl-5,7,8-trimethoxy-6-acetylchromene, there is no evidence to show whether this is due to stability of the carbinol as in acronycine, or to the pyran ring not opening.

IV. Experimental

All melting points are corrected except where otherwise stated. Microanalyses were carried out in the C.S.I.R.O. Microanalytical Laboratory.

(*a*) *Extraction and Separation of the Alkaloids.*—Milled air-dried leaves of *A. baueri* (9·6 kg.) were extracted with methanol (Soxhlet), the solution concentrated, and the residue repeatedly extracted with hot 10% hydrochloric acid. Basification with ammonia, extraction with chloroform, and repetition of treatment with hot 10% hydrochloric acid gave 130 g. crude bases. These were dissolved in hot benzene, the solution cooled, filtered, and shaken with a little water. A black tar separated at once and the benzene and water layers were decanted and kept overnight when a quantity of almost colourless crystals separated. A further quantity was obtained from the tar by passing its chloroform solution through a column of alumina, evaporating the eluate, taking up the residue in benzene, and again shaking with water. This crystalline material, identified as *2,4-dimethoxy-10-methylacridone*, is dealt with under (*b*).

The benzene solution after filtration from 2,4-dimethoxy-10-methylacridone, was extracted successively with 1% (*A*), 5% (*B*), and 20% (*C*) hydrochloric acid, six times for each acid concentration. The bases from these fractions were dissolved in benzene and by shaking with water an additional small quantity of 2,4-dimethoxy-10-methylacridone was obtained from fractions *A* and *B*. The benzene solution of fraction *A* was extracted successively with 0·02% (i), 0·05% (ii), 0·1% (iii), and 0·5% (iv) hydrochloric acid, to it was added the benzene solution of fraction *B* and the extraction continued with 1% (v) and 2% (vi) hydrochloric acid. Then was added the benzene solution of fraction *C* and extraction carried on with 5% (vii), 8% (viii), and finally 15% (ix) hydrochloric acid. The crude bases from each of fractions (i-iv) were dissolved in a little warm 2% hydrochloric acid and the acid concentration brought to *c.* 15% by addition of concentrated hydrochloric acid when kokusaginine hydrochloride crystallized, mainly from (iii) and (iv). After removing the bulk of the kokusaginine in this way, the residual bases were fractionally crystallized from ethanol, (i) and (ii) giving acronycidine, (iii) a mixture of acronycidine and skimmianine, and (iv) skimmianine. The mother liquors from each were retreated with hydrochloric acid leading to the separation of a little more kokusaginine hydrochloride after which fractional crystallization gave more skimmianine from (iv). Fractions (i), (ii), and (iii) were combined and chromatographed in benzene solution on alumina giving further quantities of kokusaginine, acronycidine, and 2,4-dimethoxy-10-methylacridone.

Solutions of fractions (v), (vi), and (vii) in benzene were run through alumina to remove dark coloured impurities, the benzene evaporated, and the bases taken up in alcohol and picrates precipitated by addition of alcoholic picric acid. Concentration yielded second crops of picrates after which unprecipitated bases were recovered from the mother liquors. In each case the picrates were separable by crystallization into the more-soluble melicopidine picrate and the less-soluble picrate of the new base *acronidine*. The mother liquors yielded the base melicopine, not precipitated by picric acid, together with further amounts of acronidine and melicopidine. Fraction (viii) dissolved in benzene was chromatographed on alumina giving a little acronidine, melicopine, and melicopidine. The bases recovered from the mother liquors were dissolved in

* The possibility of an alternative mechanism involving initial attack at C_4 and fission of the C_4-C_{10} bond is dependent on the capacity of an aldol aryl ether to split with alkali giving the phenol and two molecules of carbonyl compound—in this case acetone and acetaldehyde. However, β-methoxybutyraldehyde is not broken down to acetaldehyde.

benzene and the solution extracted successively with 5 and 15% hydrochloric acid, the former extract giving melicopidine and the latter melicopicine. Fraction (ix) consisted almost entirely of melicopicine.

The components which have been described previously were identified as follows: values in parentheses are the amounts isolated. Melicopicine (25 g.), yellow prisms from methanol, m.p. and mixed m.p. with an authentic specimen 132–133 °C.; alcoholic hydrochloric acid gave normelicopicine, orange needles from methanol, m.p. and mixed m.p. 128–129 °C. Melicopidine (13·5 g.), pale yellow prisms from methanol, m.p. and mixed m.p. 121–122 °C.; picrate, orange needles from methanol, m.p. and mixed m.p. 134–135 °C. Melicopine (1·1 g.), yellow needles from chloroform-ether, m.p. and mixed m.p. 177–178 °C. Acronycidine (0·5 g.), colourless needles from methanol, m.p. and mixed m.p. 136–137 °C.; picrate, yellow needles from methanol, m.p. and mixed m.p. 181–182 °C. Skimmianine (1·5 g.), colourless needles from methanol, m.p. and mixed m.p. 177–178 °C.; picrate, yellow needles from ethanol, m.p. 196·5–197·5 °C. Kokusaginine (4·1 g.), colourless needles from methanol, m.p. and mixed m.p. 170–171 °C. (Found: C, 65·1; H, 4·9; N, 5·3; CH_3O, 35·5%. Calc. for $C_{14}H_{13}O_4N$: C, 64·9; H, 5·0; N, 5·4; CH_3O, 35·9% (three methoxyls)). Kokusaginine picrate separated from ethanol as yellow needles, m.p. and mixed m.p. 217·5–218·5 °C.; the hydrochloride, colourless needles from 5% aqueous hydrochloric acid melted with decomposition at 225 °C. Small amounts of other basic constituents were present in some mother liquors but in amounts too small to permit of purification.

(*b*) *2,4-Dimethoxy-10-methylacridone.*—After purification through the picrate, the base crystallized from aqueous methanol as colourless needles, m.p. (after drying at 100 °C.) 163–164 °C., which did not depress the m.p. of a synthetic specimen kindly supplied by Mr. L. J. Drummond. Yield 4·5 g. (Found: C, 71·3; H, 5·5; N, 5·0; CH_3O, 22·5; CH_3N, 8·1%. Calc. for $C_{16}H_{15}O_3N$: C, 71·4; H, 5·6; N, 5·2; CH_3O, 23·0; CH_3N, 10·8%). Colourless needles of a dihydrate were obtained by shaking a benzene solution of the dimethoxyacridone with a little water (Found (on an air-dried specimen): loss of weight at 100 °C., 11·3%. Calc. for $C_{16}H_{15}O_3N.2H_2O$: 11·8%). The picrate separated from methanol as yellow needles, m.p. 205–207 °C., undepressed by admixture with the picrate of the synthetic base. The hydrochloride separated from 5% hydrochloric acid as bright yellow needles, m.p. 135–136 °C. (decomp.); it resembles melicopidine hydrochloride in that its solubility in aqueous acids is anomalous. Though not easily soluble in 1·5N, it dissolves readily in 5N hydrochloric acid. Heated at 170 °C. in an oil-bath for 5 min., the hydrochloride was demethylated giving 2-methoxy-4-hydroxy-10-methylacridone, yellow needles from aqueous ethanol, m.p. 175–176 °C. and not depressed by admixture with a synthetic specimen.

(*c*) *Acronidine.*—The base recovered from its picrate was purified by passage through a column of alumina and crystallized from methanol as large, colourless prisms, m.p. 151–153 °C. Yield 5·8 g. It is insoluble in water, moderately soluble in benzene, and very soluble in chloroform, a chloroform solution being optically inactive (Found: C, 69·5; H, 5·4; N, 4·6; CH_3O, 19·7; $CH_3(C)$, 2·4, 2·7; CH_3N, 1·7, 1·9%; mol. wt. (Rast) 315. Calc. for $C_{18}H_{17}O_4N$: C, 69·5; H, 5·5; N, 4·5; CH_3O, 19·9 (two methoxyls); $CH_3(C)$, 4·8% (one terminal methyl); mol. wt. 311). *Acronidine picrate* separated from *n*-propanol or ethanol as flat yellow needles, m.p. 216–218 °C. (decomp.) (Found: C, 53·6; H, 3·8; N, 10·3%. Calc. for $C_{18}H_{17}O_4N.C_6H_3O_7N_3$: C, 53·3; H, 3·7; N, 10·4%). Acronidine dissolves in 0·5N but is only soluble with difficulty in 0·1N hydrochloric acid. The hydrochloride separated from 2N hydrochloric acid as long cream needles which shrank at *c.* 180 °C. and decomposed gradually without melting as the temperature was raised to 320 °C.; it was not analysed. Acronidine is insoluble in aqueous alkali. It does not give a methylenedioxy test.

(*d*) iso*Acronidine.*—Acronidine (1 g.) heated in a sealed tube at 100 °C. for 4 hr. with methyl iodide (2 ml.) gave iso*acronidine*, colourless needles from ethanol, m.p. 231–232 °C. (Found: C, 69·7; H, 5·4; CH_3O, 10·3; CH_3N, 10·8%. Calc. for $C_{18}H_{17}O_4N$: C, 69·5; H, 5·5; CH_3O, 10·0 (one methoxyl); CH_3N, 9·3%).

(*e*) *Oxidation of Acronidine.*—The alkaloid was oxidized readily by permanganate in acetone but as no tractable product could be isolated the following procedure was adopted. Acronidine

(1·2 g.) was oxidized by potassium permanganate (1·8 g.) in acetone solution and the acetone evaporated under reduced pressure. The residue was stirred with sodium hydroxide solution (5%, 35 ml.) and water (200 ml.) and aqueous permanganate (3%, 180 ml.) added in 20 ml. portions during several hours. Excess permanganate was destroyed by hydrazine and the reaction mixture heated for 1 hr. on the water-bath, filtered, and the filtrate made strongly acid with hydrochloric acid. The manganese dioxide was dissolved in sulphurous acid and the resulting solution combined with the filtrate which was saturated with sodium chloride and continuously extracted with ether. The extracted acids were transferred to aqueous solution by dilute ammonia and oxalic acid removed by precipitation with calcium chloride. The filtrate from the calcium salts was reacidified and again continuously extracted with ether. The ethereal extract was dried, evaporated, and the residue sublimed (c. 100 °C., 1–2 mm.). Resublimation and crystallization from light petroleum gave colourless needles, m.p. 78–79 °C., undepressed by admixture with α-hydroxy*iso*butyric acid (Found : C, 46·8 ; H, 7·6%. Calc. for $C_4H_8O_3$: C, 46·2 ; H, 7·7%).

(*f*) *Noracronidine.*—A solution of acronidine (1·0 g.) in ethanol (15 ml.) containing hydrochloric acid (10N ; 4·5 ml.) was refluxed for 20 hr. The sparingly soluble yellow hydrochloride which separated was dissolved in dilute sodium hydroxide and the solution acidified with acetic acid giving noracronidine, colourless needles from ethanol, m.p. 256–257 °C.* Yield 0·5 g. (Found : C, 68·9 ; H, 5·0 ; N, 4·6 ; CH_3O, 10·2%. Calc. for $C_{17}H_{15}O_4N$: C, 68·7 ; H, 5·1 ; N, 4·7 ; CH_3O, 10·4%). Coupling occurred when a solution of benzene diazonium chloride was added to a solution of noracronidine in 10% sodium hydroxide, giving a reddish brown precipitate. Noracronycidine under the same conditions gave a crimson diazo-compound. *Acetyl noracronidine* separated from ethanol as colourless needles, m.p. 212–214 °C. (Found : C, 67·2 ; H, 5·2%. Calc. for $C_{19}H_{17}O_5N$: C, 67·3 ; H, 5·0%).

(*g*) *Action of Alkali on Noracronidine.*—Aqueous potassium hydroxide (30%, 30 ml.) containing noracronidine (0·5 g.) was boiled under reflux, water (20 ml.) being added at 2-hourly intervals and the same volume of liquid distilled off. The earlier distillates smelt strongly of acetaldehyde and to each distillate was added a saturated solution of 2,4-dinitrophenylhydrazine in 10% aqueous sulphuric acid until there was no further precipitation of hydrazone. Refluxing was discontinued after 12 hr. when the amount precipitated was very small. The combined dinitrophenylhydrazones (0·39 g.) were dissolved in benzene and chromatographed on alumina. The eluate was collected in six fractions, each fraction evaporated to dryness and the residues crystallized from ethanol with the following results :

Fraction	Residue	M.p. (°C.)
1	Yellow needles	122–126
2	Deep yellow needles	119–124
3	Orange-yellow needles	104–112
4	Reddish orange flat needles	128–146
5	Reddish orange flat needles	150–158
6	Reddish orange flat needles	156–160

Fraction 2 was recrystallized from the mother liquors from fraction 1, the product, m.p. 121–126 °C. was combined with fraction 1 and recrystallized from ethanol giving acetone 2,4-dinitrophenylhydrazone, m.p. 125–126 °C. undepressed by admixture with an authentic specimen (Found : C, 45·8 ; H, 4·5%. Calc. for $C_9H_{10}O_4N_4$: C, 45·4 ; H, 4·2%). Fractions 5 and 6 were combined and recrystallized first from benzene then from ethanol giving acetaldehyde 2,4-dinitrophenylhydrazone, m.p. 167–168 °C. undepressed by admixture with an authentic specimen (Found : C, 43·4 ; H, 3·6%. Calc. for $C_8H_8O_4N_4$: C, 42·9 ; H, 3·6%). The yield of mixed 2,4-dinitrophenylhydrazones was 50% on the basis of a 1 : 1 molar ratio of acetone : acetaldehyde. The proportion of each 2,4-dinitrophenylhydrazone in the mixture could not be determined but it was estimated that acetone 2,4-dinitrophenylhydrazone constituted not less than 30% and not more than 50% of the mixture. After the sixth distillation the alkaline

* This is not a good melting point, the substance melts to a thick brown gum but does not flow freely even at 300 °C.

reaction mixture was diluted with an equal volume of water and shaken with dimethyl sulphate (4 ml. in three portions). Extraction with chloroform, and evaporation of the solvent gave a crystalline solid (0·30 g.) which was redissolved in chloroform and the solution filtered through alumina. The recovered solid was crystallized first from benzene, then from water, and obtained as rosettes of short needles, m.p. 247–248 °C. (uncorr.) undepressed by admixture with *iso*-kokusaginine kindly supplied by Mr. G. K. Hughes (Found: C, 64·9; H, 5·0; N, 5·5; CH_3O, 23·6%. Calc. for $C_{14}H_{13}O_4N$: C, 64·9; H, 5·0; N, 5·4; CH_3O, 23·9% (two methoxyls)).

In a blank experiment, 0·45 g. noracronycidine, a typical methoxylated furoquinoline lacking a dimethylpyran ring, was refluxed with potassium hydroxide (30%, 30 ml.) for 2 hr., water (20 ml.) added, and then distilled off. The distillate was odourless and gave no precipitate with a solution of 2,4-dinitrophenylhydrazine in 10% aqueous sulphuric acid. From β-methoxybutyraldehyde (Heyse 1930) under the same conditions only a very small amount of 2,4-dinitrophenylhydrazones was precipitated. No acetaldehyde 2,4-dinitrophenylhydrazone was detected when the mixed dinitrophenylhydrazones were chromatographed on alumina.

(*h*) *Hydrogenation of Acronidine.*—Acronidine (1·0 g.) in ethanol (250 ml.), hydrogenated over Raney nickel, absorbed 152 ml. hydrogen at 21 °C. and 761 mm.; calculated for 2 moles, 155 ml. The solution was filtered, evaporated, and the residue dissolved in benzene and chromatographed on alumina giving two products. The first was eluted by benzene in *c.* 75% yield and crystallized from methanol as colourless needles, m.p. 192·5–194·5 °C. (Found: C, 68·5; H, 6·7; CH_3(C), 4·0, 3·8%. Calc. for $C_{18}H_{21}O_4N$: C, 68·6; H, 6·7; CH_3(C), 4·8% (one CH_3(C) group)). *Tetrahydroacronidine* (V) is insoluble in hot 4% aqueous sodium hydroxide and gives no colour with ferric chloride. It dissolves easily in cold 1% hydrochloric acid.

The second product, the *dihydropyranoquinolone* VII, was eluted by chloroform in *c.* 20% yield and crystallized from methanol as colourless, equidimensional prisms, m.p. 255–257 °C. (Found: C, 68·1; H, 7·4; N, 4·5; CH_3O, 19·3; CH_3(C), 8·6, 8·9%. Calc. for $C_{18}H_{23}O_4N$: C, 68·1; H, 7·3; N, 4·4; CH_3O, 19·6 (two methoxyls); CH_3(C), 4·7% (one CH_3(C) group)). The substance is insoluble in hot 4% aqueous sodium hydroxide and gives no colour with ferric chloride. It is only sparingly soluble in boiling 1% hydrochloric acid. The yields quoted were not reproduced. In a second experiment, there was obtained *c.* 40% tetrahydroacronidine and *c.* 57% of the higher melting substance. Tetrahydroacronidine was recovered unchanged (m.p. and mixed m.p.) after attempted hydrogenation over Raney nickel in ethanol.

(*i*) *Norskimmianine.*—Skimmianine (0·5 g.) in ethanol (20 ml.) was refluxed for 10 hr. with hydrochloric acid (10N; 4 ml.). The solid which separated on cooling was dissolved in dilute sodium hydroxide and the filtered solution acidified with acetic acid precipitating norskimmianine which crystallized from benzene or from aqueous ethanol as colourless needles, m.p. 235–236 °C. (Found: N, 5·6; CH_3O, 24·9%. Calc. for $C_{13}H_{11}O_4N$: N, 5·7; CH_3O, 25·3% (two methoxyls)). Norskimmianine couples with diazonium salts in alkaline solution to give a red precipitate.

(*j*) The ultraviolet absorption spectra were measured in ethanol solution by means of a Beckmann DU spectrophotometer. The specimen of 1-methoxy-10-methylacridone was supplied by Mr. G. K. Hughes.

V. Acknowledgments

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THE ALKALOIDS OF *CRYPTOCARYA BOWIEI* (HOOK.) DRUCE

By JEAN EWING,* G. K. HUGHES,* E. RITCHIE,* and W. C. TAYLOR*

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Summary

Two closely related water-soluble alkaloids cryptaustoline and cryptowoline iodides have been isolated from the bark of *Cryptocarya bowiei* (Hook.) Druce. Both have been shown to be derivatives of dibenzo[*b*, *g*]pyrrocoline. This constitutes the first isolation of substances containing this nucleus from natural sources.

I. INTRODUCTION

Bancroft (1887) reported the isolation of a crystalline alkaloid from the bark of *Cryptocarya australis* (Benth.), now known as *C. bowiei* (Hook.) Druce, which because of its paralytic action was thought to be related to curare. Maiden (1895) confirmed the presence of a respiratory poison and urged complete chemical investigation but this was not forthcoming until the present work was undertaken. A preliminary account of this investigation has been published (Ewing *et al.* 1952).

Stimulus was given to this project by de la Lande's (1948) isolation of the unusual vesicant alkaloid cryptopleurine from another of the Australian species, *C. pleurosperma*. Although *C. bowiei* varies in size from a small shrub in northern New South Wales and southern Queensland to a tree, about 30 ft. high, in northern Queensland it was surprising to find that the alkaloid from the southern bark samples was different from that of the northern bark samples but obviously closely related to it. Both were isolated as their sparingly soluble iodides and were optically active. Analyses indicated empirical formulae of $C_{20}H_{24}O_4NI$ (northern) and $C_{19}H_{20}O_4NI$ (southern); preliminary examination showed that these could be expanded to $C_{16}H_{11}(OH)(OCH_3)_3(NCH_3)^+I'$ and $C_{16}H_{11}(OH)(OCH_3)(O_2CH_2)(NCH_3)^+I'$ respectively. Neither gave Gibbs's reaction for phenols with a free *p*-position. It is proposed that they be called cryptaustoline and cryptowoline iodides, the latter being the one isolated from southern sources.

II. CRYPTAUSTOLINE IODIDE

By the action of methyl iodide and methanolic potassium hydroxide an *O*-methyl ether was formed in high yield and this with boiling sodium hydroxide solution gave optically active methine-I; molecular weight and analyses showed that the formula was $C_{21}H_{25}O_4N$. Catalytic hydrogenation gave dihydromethine-I, $C_{21}H_{27}O_4N$, which changed on exposure to air to a substance $C_{21}H_{25}O_4N$ referred to as dehydrodihydromethine-I, which gave a positive

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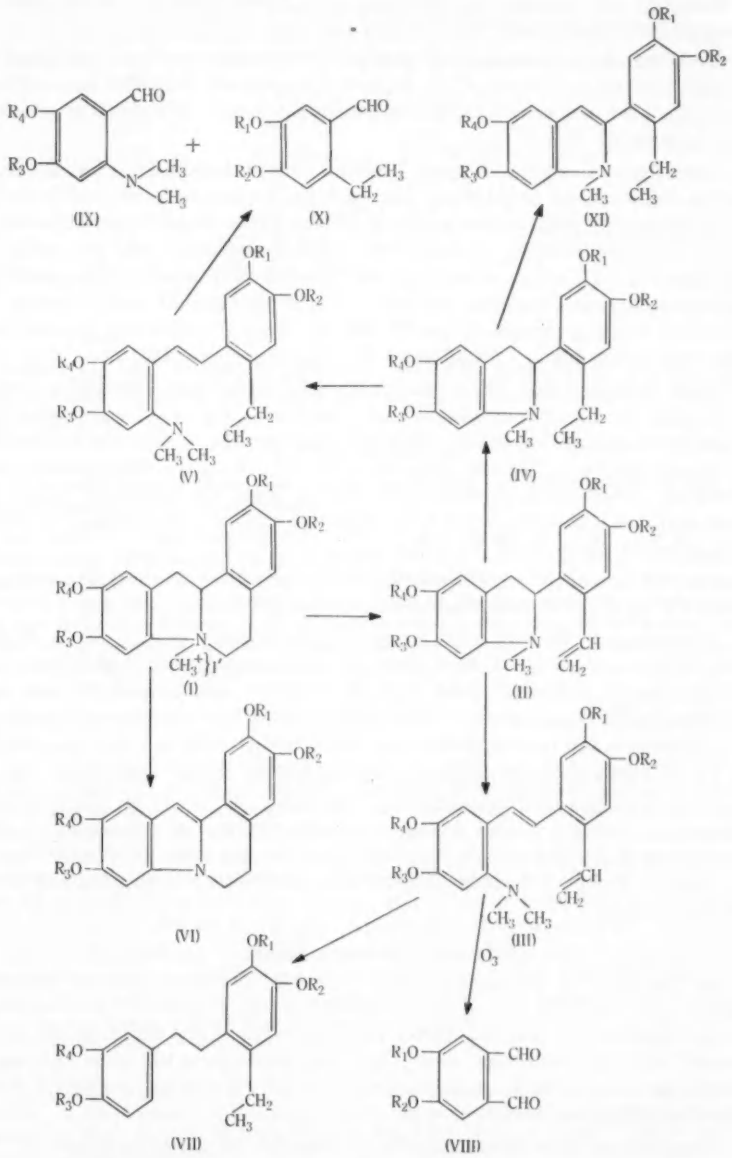

Fig. 1

Ehrlich test. Ozonolysis of methine-I gave formaldehyde showing that a terminal methylene group was present.

A Hofmann degradation of methine-I methiodide gave a high yield of optically inactive methine-II, $C_{22}H_{27}O_4N$, which could not be further exhaustively methylated, the inference being that either the nitrogen was hindered or attached to a benzene nucleus.

Ozonolysis of methine-II gave 4,5-dimethoxyphthalaldehyde but the basic fraction could not be crystallized. As methine-II contained two double bonds it was thought desirable to reduce the complexity of the ozonolysis by eliminating part of the unsaturation. Consequently dihydromethine-I was converted to dihydromethine-II, which with ozone readily afforded 6-ethylveratric aldehyde and 6-dimethylaminoveratric aldehyde. Dihydromethine-II was therefore V, methine-II was III, methine-I was II, and the *O*-methyl ether of cryptaustoline iodide was I (see Fig. 1; in all cases $R_1=R_2=R_3=R_4=CH_3$).

Both Robinson and Sugasawa (1932) and Schöpf and Thierfelder (1932) had studied the dehydrogenation of laudanosoline hoping to obtain norglaucine, a possible morphine precursor. However, the resulting dehydrolaudanosoline was shown to be I ($R_1=R_2=R_3=R_4=H$) by exhaustive methylation and ozonolysis. The second methine obtained by them was identical (m.p. and mixed m.p.) with methine-II but since their first methine was optically inactive no comparison there could be made.

Confirmation of the structure of the methyl ether was obtained by preparing VI and VII by methods described by Schöpf and Thierfelder (loc. cit.).

It remained to determine the position of the hydroxyl group. By a similar series of reactions on the *O*-ethyl ether, 6-dimethylaminoveratric aldehyde and the previously unknown 3-ethoxy-6-ethyl-4-methoxybenzaldehyde (as its semicarbazone) were obtained. This showed that the hydroxyl group is attached to the 2-position and thus cryptaustoline iodide is I ($R_1=H$, $R_2=R_3=R_4=CH_3$).

The 3-ethoxy-6-ethyl-4-methoxybenzaldehyde was prepared from 4-hydroxy-3-methoxyacetophenone by ethylation followed by Clemmensen reduction and a Gattermann aldehyde synthesis. Permanganate oxidation of it gave an acid which had the same melting point as that found by Kondo, Noto, and Tanaka (1928) for 3-ethoxy-6-ethyl-4-methoxybenzoic acid prepared by a different method.

III. Cryptowoline Iodide

At the outset it was believed that the only difference between the two alkaloids was that one had a methylenedioxy-group instead of two methoxy groups. Hence it was not unexpected that ozonolysis of the dihydromethine-II prepared from the ethyl ether of cryptowoline iodide gave the same non-basic product as above, that is, 3-ethoxy-4-methoxy-6-ethylbenzaldehyde and 6-dimethylaminopiperonal.

The structure of cryptowoline iodide is therefore as shown in Figure 2.

The 6-dimethylaminopiperonal was prepared by methylation of 6-amino-piperonylidene-*p*-toluidine.

Finally the isolation of these two alkaloids provides the first confirmation of the prediction of Schöpf and Thierfelder (1932) that alkaloids having the dibenzopyrrocolinium nucleus should occur in the plant cell. Folkers, Koniuszy,

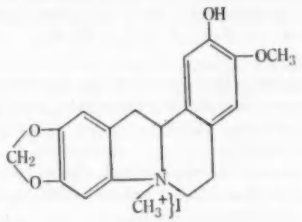

Fig. 2

and Shavel (1951) suggested structures with this nucleus for the erythrina alkaloids but Carmack, McKusick, and Prelog (1951) have thrown doubt on this hypothesis.

IV. Experimental

All melting points are uncorrected. Analyses are by K. W. Zimmerman, C.S.I.R.O., and Mrs. E. Reichert, University of Sydney.

(*a*) *Isolation of Cryptaustoline Iodide.*—The ground bark (12 kg.), from trees growing at Mossman Gorge, north Queensland, was exhausted with cold methanol (6×5 l.). The combined extracts were concentrated to 1·5 l., thoroughly mixed with dilute acetic acid (3 l. of 2%), filtered, saturated with potassium iodide (300 g.), and set aside. The supernatant liquid was decanted and extracted with chloroform (9×2 l.). After removal of the solvent the residue was added to the gummy precipitate and dissolved in hot methanol (800 ml.). On standing *cryptaustoline iodide* was obtained as small prisms which after several recrystallizations from methanol had m.p. 214 °C. (decomp.), $[\alpha]_D^{20°}$ —151° (*c*, 0·4% in ethanol). Yield 80 g. (Found: C, 51·0; H, 5·3; N, 3·0; CH_3O, 19·5%. Calc. for $C_{20}H_{24}O_4NI$: C, 51·1; H, 5·4; N, 3·0; 3×CH_3O, 19·8%).

(*b*) O-*Methylcryptaustoline Iodide.*—Cryptaustoline iodide (40 g.) dissolved in methanolic potassium hydroxide (400 ml. of 0·5N) and methyl iodide (25 ml.) were refluxed for 6 hr. and the mixture then concentrated to 100 ml. After removing the potassium iodide the solution was further concentrated, cooled, the methyl derivative collected and crystallized from water (300 ml.) as white rods (36 g., 85%), m.p. 80–90 °C. It was obviously a hydrate and no satisfactory analyses could be obtained even on carefully dried material of m.p. 153–155 °C., $[\alpha]_D^{20°}$—175° (*c*, 0·4% in ethanol) (Found: C, 47·1; H, 5·6; N, 3·1; CH_3O, 23·0; H_2O, 8·2%. Calc. for $C_{21}H_{26}O_4NI.2H_2O$: C, 47·6; H, 5·0; N, 2·7; 4×CH_3O, 23·6; H_2O, 8·5%).

(*c*) O-*Methyl Methine*-I.—A solution of *O*-methylcryptaustoline iodide (15 g.) and sodium hydroxide (90 g.) in water (700 ml.) was refluxed for 1·5 hr. by which time large oily drops had formed. These were transferred to ether, dried, and distilled under reduced pressure to produce a clear glass which crystallized from methanol as colourless needles (9 g., 90%), m.p. 101 °C., $[\alpha]_D^{20°}$—221° (*c*, 0·4% in chloroform) (Found: C, 71·1; H, 7·1; CH_3O, 34·5%. Calc. for $C_{21}H_{25}O_4N$: C, 71·0; H, 7·0; 4×CH_3O, 34·9%).

The *methiodide* was prepared by heating the base and methyl iodide in a sealed tube at 100 °C. for 3 hr. It was recrystallized from methanol-ether as colourless prisms (yield 84%), m.p. 195 °C. (Found: C, 53·0; H, 5·7; N, 3·0; CH_3O, 34·7%. Calc. for $C_{22}H_{28}O_4NI$: C, 53·1; H, 5·7; N, 2·8; 4×CH_3O; 34·9%).

(*d*) O-*Methyl Methine*-II.—The above iodide (8 g.) and sodium hydroxide solution (300 ml. of 13%) were refluxed for 1·5 hr., cooled, and the lemon-yellow oil extracted with ether. The

solvent was removed from the dried extract and the residue crystallized from methanol (30 ml.) as pale lemon needles (4·5 g.), m.p. 111 °C., $[\alpha]_D^{20}0°$ (Found : C, 71·8 ; H, 7·5 ; N, 4·1 ; CH_3O, 33%. Calc. for $C_{22}H_{27}O_4N$: C, 71·7 ; H, 7·4 ; N, 3·8 ; $4\times CH_3O$, 33·6%).

The *methiodide*, the formation of which required a large excess of methyl iodide and prolonged heating, was obtained as microprisms, m.p. 188 °C. (Found : C, 54·0 ; H, 6·1 ; CH_3O, 24·6%. Calc. for $C_{23}H_{30}O_4NI$: C, 53·8 ; H, 6·1 ; $4\times CH_3O$, 24·4%). It was unaffected after heating with sodium hydroxide for 2 hr.

(*e*) O-*Methyl Tetrahydromethine*-II.—Prepared by catalytic hydrogenation of *O*-methyl methine-II in presence of Raney nickel. It crystallized from a small volume of ethanol as colourless needles, m.p. 64 °C. (Found : C, 70·5 ; H, 7·8 ; CH_3O, 33·1%. Calc. for $C_{22}H_{31}O_4N$: C, 70·7 ; H, 8·4 ; $4\times CH_3O$, 33·2%).

The *methosulphate* was prepared in benzene and crystallized from methanol-ether as microneedles, m.p. 197 °C. (Found : C, 57·9 ; H, 7·1 ; N, 2·8 ; CH_3O, 31·0%. Calc. for $C_{24}H_{37}O_8NS$: C, 57·7 ; H, 7·4 ; N, 2·8 ; $5\times CH_3O$, 31·0%).

(*f*) O-*Methyl Dihydromethine*-I.—The methine-I was hydrogenated at room temperature in presence of Raney nickel. The dihydro-derivative was recrystallized from aqueous ethanol as colourless needles, m.p. 67 °C. but was too unstable for analysis.

The *methiodide* prepared from freshly prepared base was recrystallized from methanol-ether as prisms, m.p. 201 °C. (Found : C, 52·1 ; H, 6·1 ; N, 2·8 ; CH_3O, 24·2%. Calc. for $C_{22}H_{30}O_4NI$: C, 52·4 ; H, 6·1 ; N, 2·8 ; $4\times CH_3O$, 24·8%). After long standing in solution the dihydromethine was converted to a less soluble compound which was finally crystallized from methanol as off-white prisms, m.p. 131 °C. This gave an intense indole reaction with Ehrlich's reagent and was evidently the dehydrodihydromethine (XI) (Found : C, 70·8 ; H, 6·9 ; CH_3O, 33·8%. Calc. for $C_{21}H_{25}O_4N$: C, 71·0 ; H, 7·1 ; $4\times CH_3O$, 34·9%).

(*g*) O-*Methyl Dihydromethine*-II.—Dihydromethine-I methiodide (3·2 g.), sodium hydroxide solution (150 ml. of 20%), and ethanol (10 ml.) were refluxed for 3 hr. The product, isolated as above, crystallized from ethanol (15 ml.) as needles (2·2 g.), m.p. 120 °C. (Found : C, 71·3 ; H, 7·2 ; N, 4·1 ; CH_3O, 33·3%. Calc. for $C_{22}H_{29}O_4N$: C, 71·1 ; H, 7·8 ; N, 3·8 ; $4\times CH_3O$, 33·4%).

(*h*) *Ozonolysis of* O-*Methyl Methine*-I.—The methine, dissolved in freshly distilled carbon tetrachloride, was ozonized at —20 °C. After removing the solvent *in vacuo* the residue was refluxed with water and then distilled into alcoholic dimedon. The precipitate (20% yield) was collected and recrystallized from ethanol, m.p. 188 °C. undepressed on admixture with formaldehyde dimedon.

(*i*) *Ozonolysis of* O-*Methyl Methine-II*.—An ethyl acetate solution of methine-II was ozonized at —20 °C. The solvent was removed *in vacuo* and the partially crystalline residue, which gave aldehyde reactions, was dissolved in ethanol. On cooling pale brown needles of 4,5-dimethoxyphthalaldehyde deposited and were recrystallized from water as straw coloured flakes (yield 38%), m.p. 170 °C. (Found : C, 61·6 ; H, 5·4 ; CH_3O, 31·4%. Calc. for $C_{10}H_{10}O_4$: C, 61·8 ; H, 5·2 ; $2\times CH_3O$, 31·8%). This aldehyde (0·15 g.) in water (40 ml.) was oxidized with potassium permanganate solution (1·5 ml. of 10%). The acid, isolated in the usual manner, crystallized from chloroform, m.p. 198–199 °C. (0·08 g., 57%). This was converted to the ethylimide, yellow needles from methanol, m.p. 228 °C. Perkin (1916) gave m.p. 228 °C. for the ethylimide of *m*-hemipinic acid (Found : C, 61·0 ; H, 5·3%. Calc. for $C_{12}H_{13}O_4N$: C, 61·2 ; H, 5·5%). The basic fraction from the ozonolysis was intractable.

(*j*) *Ozonolysis of* O-*Methyl Dihydromethine-II*.—A solution of the dihydromethine (1·0 g.) in water (130 ml.), sulphuric acid (10 ml. of 2N), and acetic acid (7 ml.) was ozonized for 40 min., the solution being extracted with ether (100 ml.) at 10-min. intervals (ether extract *A*).

The aqueous solution was shaken with palladized charcoal and hydrogen for 15 min., filtered, made strongly alkaline, and extracted with ether. The solvent was removed from the dried extract and the oily residue crystallized from light petroleum as yellow needles, m.p. 71 °C. (0·17 g., 30%) (Found : C, 63·2 ; H, 6·8 ; N, 7·0 ; CH_3O, 29·3%. Calc. for $C_{11}H_{15}O_3N$: C, 63·1 ; H, 7·2 ; N, 6·8 ; $2\times CH_3O$, 29·6%). Schöpf and Thierfelder (loc. cit.) report that 6-dimethylaminoveratric aldehyde has m.p. 71 °C.

The extract *A* was washed with dilute acid and alkali, dried, and distilled *in vacuo* to give a pale yellow oil, b.p. 170–180 °C./1 mm. (bath temp.) which solidified at 0 °C. and remelted at about 26 °C. It gave a semicarbazone, colourless needles from aqueous ethanol, m.p. 198 °C. (Found: C, 57·3; H, 6·5; N, 16·4; CH_3O, 24·7%. Calc. for $C_{12}H_{17}O_3N_3$: C, 57·3; H, 6·8; N, 16·8; $2\times CH_3O$, 24·7%). 6-Ethylveratric aldehyde semicarbazone has m.p. 198 °C. (Barger and Silberschmidt 1928).

(*k*) *Emde Degradation of* O-*Methyl Tetrahydromethine-II Methosulphate.*—The methosulphate (0·55 g.) in water (25 ml.) was heated on the steam-bath with sodium amalgam (20 g. of 5%) for 2 hr. The oil which separated was taken up in ether, washed with dilute hydrochloric acid to remove unchanged material (0·15 g.), and then dried. After removal of the solvent the oily residue was crystallized from aqueous ethanol as needles, m.p. 78 °C. (0·2 g., 52%) (Found: C, 73·0; H, 7·9; CH_3O, 37·1%. Calc. for $C_{20}H_{26}O_4$: C, 72·7; H, 7·9; $4\times CH_3O$, 37·6%). This substance was identical (m.p. and mixed m.p.) with tetrahydrolaudanosene, 6′-ethyl-3,4,3′,4′-tetramethoxy-αβ-diphenylethane, (VII) prepared from laudanosine after the method of Decker and Galatty (1909) using the methiodides instead of the methosulphates throughout (cf. Robinson and Sugasawa).

(*l*) *6-Dimethylamino-3,4,3′,4′-tetramethoxy-6-vinyl Stilbene.*—This was prepared from papaverine through tetramethyldehydrolaudanosoline by a combination of the methods of Robinson and Sugasawa (loc. cit) and Schöpf and Thierfelder. Its m.p. 110 °C. was undepressed on admixture with *O*-methyl methine-II.

(*m*) *Des-N-methyl-O-methyl Cryptaustoline.*—*O*-Methyl cryptaustoline chloride (from the iodide, 0·4 g.) was gradually heated to 200 °C. under vacuum (0·6 mm.) and then at 220 °C. for 3 min. The clear greenish yellow oil was recrystallized five times from methanol as grey-green flakes, m.p. 200 °C. Yield 0·08 g., 35% (Found: C, 70·8; H, 6·3; N, 4·4; CH_3O, 36·1%. Calc. for $C_{20}H_{21}O_4N$: C, 70·8; H, 6·3; N, 4·2; $4\times CH_3O$, 36·5%). It gave a royal blue colour with Ehrlich's reagent and was identical (m.p. and mixed m.p.) with 2,3,9,10-tetramethoxy-dihydrodibenzopyrrocoline prepared from tetramethyldehydrolaudanosoline (Schöpf and Thierfelder 1932).

(*n*) *The Ethyl Series.*—These compounds were prepared by essentially the same methods as for the corresponding methyl derivatives and are thus listed as briefly as possible.

(i) O-*Ethyl Cryptaustoline Iodide.* Colourless blades from water, m.p. 90–95 °C. Satisfactory analysis could not be obtained, the following is on material dried *in vacuo* at 60 °C. (Found: CH_3O, 24·7%. Calc. for $C_{22}H_{28}O_4NI$: $3\times CH_3O$, $1\times C_2H_5O$ as CH_3O, 25·0%).

(ii) O-*Ethyl Methine-I.* Colourless prisms from methanol, m.p. 104 °C. (Found: C, 71·7; H, 7·2%. Calc. for $C_{22}H_{27}O_4N$: C, 71·8; H, 7·4%). The *methiodide* crystallized as prisms from methanol, m.p. 200 °C. (Found: N, 3·1%. Calc. for $C_{23}H_{30}O_4NI$: N, 2·8%).

(iii) O-*Ethyl Dihydromethine-I.* Colourless rectangular plates from methanol, m.p. 107 °C. (Found: C, 71·4; H, 7·8; N, 4·1%. Calc. for $C_{22}H_{29}O_4N$: C, 71·1; H, 7·8; N, 3·8%). The *methiodide* formed colourless plates, m.p. 203 °C. (Found: C, 53·9; H, 6·3; N, 2·6%. Calc. for $C_{23}H_{32}O_4NI$: C, 53·8; H, 6·3; N, 2·7%).

(iv) O-*Ethyl Methine-II.* Lemon-green fluorescent prisms from ethanol, m.p. 115–116 °C. (Found: C, 72·1; H, 7·5%. Calc. for $C_{23}H_{29}O_4N$: C, 72·0; H, 7·6%).

(v) O-*Ethyl Dihydromethine-II.* Rods with pale blue fluorescence from methanol, m.p. 109 °C. (Found: C, 71·5; N, 7·8%. Calc. for $C_{23}H_{31}O_4N$: C, 71·6; H, 8·1%).

(*o*) *Ozonolysis of* O-*Ethyl Dihydromethine-II.*—The basic product had m.p. 71 °C., undepressed on admixture with the compound obtained from the corresponding methyl derivative. The neutral aldehyde yielded a semicarbazone, fluffy needles from aqueous ethanol, m.p. 183 °C. (Found: C, 58·8; H, 7·4; N, 15·8%. Calc. for $C_{13}H_{19}O_3N_3$: C, 58·9; H, 7·2; N, 15·8%).

(*p*) *4-Ethoxy-3-methoxyethylbenzene.*—4-Ethoxy-3-methoxyacetophenone (6·5 g.) was added to a boiling mixture of amalgamated zinc turnings (32 g.), water (25 ml.), and concentrated hydrochloric acid (25 ml.) during 30 min. The mixture was refluxed for a further 4 hr. The product, isolated in the usual way, was a clear colourless liquid (4·5 g.), b.p. 92–94 °C./1 mm, Kondo, Noto, and Tanaka (1928) give b.p. 95 °C./5 mm.

(*q*) *3-Ethoxy-6-ethyl-4-methoxybenzaldehyde.*—A rapid stream of dry hydrogen chloride was passed into an ice-cooled and vigorously stirred mixture of 3-ethoxy-4-methoxyethylbenzene (3·7 g.), zinc cyanide (3·7 g.), and benzene (25 ml.) for 30 min. Powdered aluminium chloride (3·5 g.) was then added gradually and the stirring continued for 2 hr. After adding ice and dilute hydrochloric acid, the unchanged ether was removed in steam. The aldehyde, isolated by ether extraction and distillation (b.p. 140–142 °C./1 mm.) crystallized from light petroleum (40–60 °C.) as off-white needles, m.p. 80 °C. (0·8 g., 20%) (Found: C, 69·5; H, 7·6%. Calc. for $C_{12}H_{16}O_3$: C, 69·3; H, 7·7%). The semicarbazone was crystallized from aqueous ethanol as needles, m.p. 183 °C. undepressed by admixture with the semicarbazone described in Section IV (*o*) (Found: C, 59·2; H, 7·2; N, 15·7%. Calc. for $C_{13}H_{19}O_3N_3$: C, 58·9; H, 7·2; N, 15·8%). The aldehyde was oxidized by potassium permanganate in acetone to the acid, needles from water, m.p. 139 °C. Kondo, Noto, and Tanaka (1928) found m.p. 138 °C. for 3-ethoxy-6-ethyl-4-methoxybenzoic acid. This acid also obtained from the aldehyde described in Section IV (*o*) (Found: C, 64·3; H, 6·7%. Calc. for $C_{12}H_{16}O_4$: C, 64·3; H, 7·0%).

(*r*) *Isolation of Cryptowoline Iodide.*—The bark (4 kg.), obtained from trees growing at North Brookfield in southern Queensland, was extracted as in Section IV (*a*). The iodide after several recrystallizations from methanol was obtained as off-white prisms, m.p. 245–246 °C. (45 g., 1·1%), $[\alpha]_D^{20°}$—186° (*c*, 0·4% in ethanol) (Found: C, 50·3; H, 4·5; N, 3·1; CH_3O, 7·8%. Calc. for $C_{19}H_{20}O_4NI$: C, 50·2; H, 4·5; N, 3·1; $1\times CH_3O$, 6·9%).

(*s*) O-*Methyl Cryptowoline Iodide.*—Colourless triangular prisms were crystallized from water, m.p. 227 °C., $[\alpha]_D^{20°}$—179° (*c*, 0·4% in ethanol) (Found: C, 51·5; H, 4·9; N, 3·1; CH_3O, 13·4%. Calc. for $C_{20}H_{22}O_4NI$: C, 51·3; H, 5·0; N, 3·0; $2\times CH_3O$, 13·3%).

(*t*) O-*Methyl Methine-I.*—It formed a colourless glass, b.p. 238–240 °C./1 mm. which could not be crystallized, $[\alpha]_D^{25°}$—172° (*c*, 0·85% in chloroform).

The *methiodide* crystallized from methanol-ether as rectangular plates, m.p. 185 °C. (Found: C, 52·2; H, 5·1; N, 2·9; CH_3O, 12·9%. Calc. for $C_{21}H_{24}O_4NI$: C, 52·3; H, 5·1; N, 2·9; $2\times CH_3O$, 12·9%).

The dihydro-derivative could not be crystallized but its methiodide formed colourless cubes, m.p. 198 °C. (Found: C, 52·2; H, 5·5; CH_3O, 13·1%. Calc. for $C_{21}H_{26}O_4NI$: C, 52·2; H, 5·4; $2\times CH_3O$, 12·9%).

(*u*) O-*Methyl Methine-II.*—Lemon-yellow plates formed from methanol, m.p. 114 °C. (Found: C, 71·7; H, 6·7; N, 4·2; CH_3O, 18·3%. Calc. for $C_{21}H_{23}O_4N$: C, 71·4; H, 6·6; N, 4·0; $2\times CH_3O$, 17·6%).

(*v*) O-*Ethyl Cryptowoline Iodide.*—Colourless prisms crystallized from methanol, m.p. 215 °C. (Found: C, 51·7; H, 5·1; N, 3·3; CH_3O, 13·5%. Calc. for $C_{21}H_{24}O_4NI$: C, 52·1; H, 5·1; N, 3·3; $1\times CH_3O+1\times C_2H_5O$, 13·0%). This was converted to the methine which could not be crystallized.

(*w*) O-*Ethyl Dihydromethine-II.*—The product formed white needles, m.p. 102 °C. Its solution possessed a deep blue fluorescence (Found: C, 71·5; H, 7·4%. Calc. for $C_{22}H_{27}O_4N$: C, 71·5; H, 7·4%). Ozonolysis, as above, gave a non-basic aldehyde, the semicarbazone of which had m.p. 183 °C. undepressed on admixture with the semicarbazone prepared in Section IV (*q*). The basic fraction crystallized in yellow leaflets, m.p. 92 °C. (yield 30%). It gave a positive Labat methylenedioxy test (Found: C, 62·2; H, 5·9; N, 7·7%. Calc. for $C_{19}H_{11}O_3N$: C, 62·1; H, 5·7; N, 7·3%).

(*x*) *6-Dimethylaminopiperonal.*—This was prepared from 6-aminopiperonylidene-*p*-toluidine (Rilliet and Kreitmann 1921) using the methylation process of Schöpf and Thierfelder (loc. cit.). The crude product, dissolved in benzene, was run through a column of alumina. After several recrystallizations from light petroleum (40–60 °C.) it had m.p. 92 °C., undepressed by admixture with the substance described in the previous section (Found: N, 7·5%. Calc. for $C_{19}H_{11}O_3N$: N, 7·3%).

V. Acknowledgments

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THE CHEMICAL CONSTITUENTS OF AUSTRALIAN *ZANTHOXYLUM* SPECIES

II. THE CONSTITUENTS OF Z. BRACHYACANTHUM F. MUELL., Z. VENEFICUM F. M. BAIL., AND Z. SUBEROSUM C. T. WHITE

By J. R. CANNON,* G. K. HUGHES,* E. RITCHIE,* and W. C. TAYLOR*

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Summary

The known substances *l*-α-canadine methiodide, β-homochelidonine, chelerythrine, *iso*corydine methiodide (a new alkaloid), lupeol, and hesperidin have been isolated from both *Z. brachyacanthum* F. Muell. and *Z. veneficum* F. M. Bail. and it is suggested that these two species are identical. From *Z. suberosum* C. T. White the recently discovered alkaloid, canthin-6-one, was isolated.

I. INTRODUCTION

Jowett and Pyman (1913) reported the isolation of *l*-α-canadine methiodide and γ-homochelidonine from the bark of *Zanthoxylum brachyacanthum* F. Muell. but as this species and also *Z. veneficum* F. M. Bail. have yellow bark and wood reminiscent of other Australian rutaceous species, which had yielded the acridone alkaloids, it was thought desirable to reinvestigate them. This was further justified because their procedure would not have extracted any weakly basic material.

In Part I of this series (Ewing, Hughes, and Ritchie 1950) it was mentioned that the bark of *Z. suberosum* C. T. White gave positive alkaloid tests and in this paper the isolation and characterization of the base are given.

II. THE CONSTITUENTS OF Z. BRACHYACANTHUM AND Z. VENEFICUM

The first of the above species is found in southern Queensland and northern New South Wales and the latter is confined to the Atherton Tableland area of northern Queensland. The barks of both yielded the known alkaloids β-homochelidonine,† *l*-α-canadine (as found by Jowett and Pyman loc. cit.), chelerythrine, a new alkaloid subsequently identified as *iso*corydine methiodide, $C_{21}H_{26}O_4NI$ (*iso*corydine itself is a known alkaloid), along with the triterpene alcohol, lupeol, and the glycoside, hesperidin. From the leaves of each species small quantities of β-homochelidonine only were isolated.

Because there was such complete correspondence in constituents of these two species several samples from different areas were examined. In all cases the same constituents were found although there was some variation in relative amounts which is probably connected with the size of the tree.

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† This is a polymorphous form of γ-homochelidonine.

This led us to suggest that *Z. brachyacanthum* and *Z. veneficum* are identical and Mr. L. H. Smith of the Queensland Herbarium has recently stated " that at present there is considerable doubt that these two are distinct species but examination of further flowering material is necessary before a final decision can be reached."

The *iso*corydine methiodide was identified as follows. It gave a positive Gibbs test for phenols with a free *p*-position and readily formed an *O*-methyl ether which was identical with the *O*-methyl ether of corydine methiodide. Infra-red spectra confirmed this and also showed that the two isomeric unmethylated compounds were different. Further, both of the methyl ethers were degraded by exhaustive methylation to 3,4,5,6-tetramethoxy-1-vinylphenanthrene as described by Gadamer (1911).

III. The Constituents of Z. suberosum

No new compounds were obtained from the bark but it was a coincidence that a good yield of the alkaloid, canthin-6-one, was obtained. This was only recently identified by Haynes, Nelson, and Price (1952) in another Australian species, *Pentaceras australis* Hook. f.

A thorough examination of the leaves gave no alkaloid nor could any other crystalline substance be separated.

IV. Experimental

(*a*) *Extraction of the Bark of* Z. veneficum.—The milled bark (3·8 kg.), from trees growing near Wongabel, Queensland, was exhausted with light petroleum (b.p. 40–80 °C.) and then with methanol. The former on concentration yielded lupeol (0·2%), m.p. and mixed m.p. 213–214 °C., $[\alpha]_D^{18°}$ +27·1° (*c*, 3·3% in $CHCl_3$) (lit. m.p. 213 °C., $[\alpha]_D$ +27·4° (*c*, 9·5% in $CHCl_3$)). Its benzoate had m.p. and mixed m.p. 267–269 °C., $[\alpha]_D^{18°}$ +62·9° (*c*, 0·9% in $CHCl_3$) (lit. 266 °C., $[\alpha]_D$ +61·2° (*c*, 3·1% in $CHCl_3$)). The methanolic extract on standing deposited fine white needles which after recrystallization from methanol gave hesperidin (0·05%), m.p. 260 °C. (decomp.). It gave an acetate, m.p. 179–180 °C. undepressed by authentic hesperidin octaacetate.

The mother liquors were concentrated and extracted with 5% hydrochloric acid. The acid solution was basified with ammonia, and the precipitate transferred to ether which was dried and evaporated. The residue, dissolved in benzene, was passed through a column of alumina and β-homochelidonine (0·03%), m.p. 161–162 °C. (lit. 159–160 °C.) was obtained from the concentrated eluate (Found : C, 68·0 ; H, 6·4 ; N, 3·9 ; CH_3O, 16·6%. Calc. for $C_{21}H_{23}O_5N$: C, 68·3 ; H, 6·3 ; N, 3·8 ; $2\times CH_3O$, 16·8%). The picrate, yellow needles from ethanol had m.p. 205–207 °C. (lit. 207–208 °C.) (Found : N, 9·2%. Calc. for $C_{27}H_{26}O_{12}N_4$: N, 9·4%). The hydrochloride formed colourless needles, m.p. 188–192 °C. (lit. 190 °C.) (Found : Cl, 8·8%. Calc. for $C_{21}H_{23}O_5N.HCl$: Cl, 8·5%). From some of the residues blunt needles, m.p. 172–173 °C. were obtained and identified as γ-homochelidonine ; they could be converted to the β-compound by seeding a solution with the latter.

The residual ammoniacal solution was acidified and mercuric chloride added. The precipitate was collected, washed, decomposed with hydrogen sulphide, and filtered. The clear filtrate was saturated with potassium iodide and the precipitated gum on repeated recrystallization from methanol yielded *iso*corydine methiodide (0·4%) and the more soluble *l*-α-canadine methiodide (0·3%), $[\alpha]_D^{22°}$ —115·6° (*c*, 0·3% in H_2O), ($[\alpha]_D$ calculated from the literature value of chloride would be —111°), which melted at 218 °C. then resolidified, and again melted at 245 °C. (decomp.). Jowett and Pyman record 220 °C. then 250 °C. (decomp.) (Found : C, 52·3 ; H, 5·0 ;

N, 2·9; I, 26·1; CH_3O, 13·1%. Calc. for $C_{21}H_{24}O_4NI$: C, 52·4; H, 5·0; N, 2·9; I, 26·4; $2\times CH_3O$, 12·9%).

The original residue, left after acid extraction, was stirred with dilute ammonia, dried, and then heated with 10% acetic acid. The yellow solution was basified and extracted with chloroform. After removal of the solvent the residue, dissolved in benzene, was chromatographed on alumina. A bright yellow band on elution yielded chelerythrine (0·06%) colourless needles from benzene, m.p. 257–259 °C., from alcohol as the solvate, m.p. 204–206 °C. (lit. m.p. 207 °C.) (Found: C, 69·3; H, 5·9; N, 3·7; CH_3O, 24·1%. Calc. for $C_{21}H_{19}O_4N.C_2H_5OH$: C, 70·2; H, 5·9; N, 3·6; $3\times CH_3O$, 24·1%). The hydrochloride formed golden-yellow needles from water, m.p. 202–203 °C. (decomp.) (Found: C, 53·8; H, 5·9; Cl, 7·6; H_2O, 19·4%. Calc. for $C_{21}H_{18}O_4N.HCl.5H_2O$: C, 53·4; H, 6·0; Cl, 7·5; $5H_2O$, 19·4%). The ψ-cyanide recrystallized from ethanol, m.p. 256–257 °C. (decomp.) or from acetone, m.p. 261–263 °C. Gadamer and Stichel (1924) recorded m.p. 256 °C. from chloroform-alcohol and Späth and Küffner (1931), m.p. 260–261 °C. from acetone.

(*b*) *Identification of* iso*Corydine Methiodide.*—It formed colourless needles from ethanol, m.p. 228 °C. (decomp.), Schlittler and Huber (1952) record m.p. 224–225 °C. for *iso*corydine methiodide, $[\alpha]_D^{23°}$ +136·3° (*c*, 0·5% in H_2O (lit. $[\alpha]_D$ +143·3° (*c*, 1% in H_2O)) (Found: C, 52·3; H, 5·6; N, 2·7; I, 26·0; CH_3O, 19·5%. Calc. for $C_{21}H_{26}O_4NI$: C, 52·3; H, 5·5; N, 2·9; I, 26·2; $3\times CH_3O$, 19·3%). It gave a negative test for a methylenedioxy-group and a brilliant blue colour with 2,6-dibromoquinone chlorimide indicating a phenol with a free *p*-position. On treatment with methyl sulphate and sodium hydroxide an iodide, m.p. 258 °C. (decomp.), $[\alpha]_D^{25°}$ +180·4° (*c*, 0·48% in H_2O) was eventually obtained. The m.p. was undepressed on admixture with an authentic specimen of *O*-methyl corydine methiodide (Found: C, 53·3; H, 5·6; N, 2·6; I, 25·3; CH_3O, 24·9%. Calc. for $C_{22}H_{28}O_4NI$: C, 53·3; H, 5·7; N, 2·8; I, 25·8; $4\times CH_3O$, 24·9%). The identify of these two compounds was further established by converting each by exhaustive methylation to the known 3,4,5,6-tetramethoxy-1-vinylphenanthrene, m.p. 69 °C. (lit. 69 °C.) (Found: C, 74·0; H, 6·3%. Calc. for $C_{20}H_{20}O_4$: C, 74·0; H, 6·2%). In this degradation it was found that the first methine, a mixture, which could not be crystallized, gave two crystalline *methiodides* as expected,* when its ethereal solution was treated with methyl iodide. The β-compound (60% yield) separated out first and was optically inactive.

The α-methine methiodide formed colourless needles from methanol-ethyl acetate, m.p. 168 °C. $[\alpha]_D^{20°}$ —160° (*c*, 0·3% in ethanol) (Found: C, 54·2; H, 6·0%. Calc. for $C_{23}H_{30}O_4NI$: C, 54·0; H, 5·9%). The β-methine methiodide crystallized from ethanol in colourless flakes, m.p. 278–280 °C. (decomp.) (Found: C, 54·0; H, 6·1%. Calc. for $C_{23}H_{30}O_4NI$: C, 54·0; H, 5·9%).

(*c*) *Extraction of the Bark of* Z. brachyacanthum.—The bark from trees growing near Brisbane, Queensland, was examined as above. The products found were *l*-α-canadine methiodide (1%), *iso*corydine methiodide (0·7%), chelerythrine (0·05%), β-homochelidonine (0·01%), lupeol (0·1%), and hesperidin (0·02%).

(*d*) *Extraction of the Leaves of* Z. brachyacanthum *and* Z. veneficum.—The only product isolated in each case was β-homochelidonine (0·01%).

(*e*) *Extraction of the Bark of* Z. suberosum.—The concentrated alcoholic extract of the bark (3 kg.) was treated with warm 5% hydrochloric acid which was then exhausted with chloroform. The solvent was evaporated, the weakly basic residue dissolved in benzene, and the solution passed through a column of alumina. From the eluate crude canthin-6-one was obtained, which recrystallized from methanol as colourless needles (0·45%), m.p. 158–159 °C. undepressed on admixture with an authentic specimen (Found: C, 76·1; H, 3·8; N, 12·8%. Calc. for $C_{14}H_8ON_2$: C, 76·4; H, 3·7; N, 12·7%). The hydrochloride was obtained as pale yellow

* Gadamer (1911) gave m.p. 260 °C. for a methine methiodide and later (1915) recorded $[\alpha]_D$ —220–225° for a methosulphate.

laths from 5% hydrochloric acid and melted between 220–230 °C. (Found : C, 54·1 ; H, 5·0 ; N, 9·3%. Calc. for $C_{14}H_8ON_2.HCl.3H_2O$: C, 54·1 ; H, 4·9 ; N, 9·0%).

(*f*) *The Action of Sodium Hydroxide on Canthin-6-one.*—(i) Following the method of Haynes, Nelson, and Price (loc. cit.) *cis*-β-carbolinyl-1-acrylic acid, m.p. and mixed m.p. 208–210 °C. was obtained.

(ii) Canthin-6-one (1 g.) was refluxed with aqueous sodium hydroxide (200 ml. of 20%) for 3 hr. Acidification yielded a flocculent yellow precipitate which on recrystallization from water formed small yellow needles, m.p. 275–277 °C. (decomp.) of the *trans*-acid (Found : C, 67·9 ; H, 4·5 ; N, 11·4%. Calc. for $C_{14}H_{10}O_2N_2.\frac{1}{2}H_2O$: C, 68·0 ; H, 4·5 ; N, 11·3%).

V. Acknowledgments

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SHORT COMMUNICATIONS

THE CONSTITUENTS OF *LEGNEPHORA MOOREI* F. MUELL.*

By G. K. HUGHES,† F. P. KAISER,† N. MATHESON,† and E. RITCHIE†

Legnephora moorei F. Muell., family Menispermaceae, is a robust vine with stems and roots up to 9 in. in diameter, which occurs infrequently in the rain-forest and " dry " rain-forest areas of eastern Australia. A Prollius extract of the root-bark gave faintly positive alkaloid tests, but strong tests were obtained on a 2 per cent. hydrochloric acid extract. These preliminary tests indicated that a water-soluble quaternary alkaloid was probably present and this was confirmed by a large-scale extraction which yielded *iso*corydine methiodide. It is interesting to note that the first natural occurrence of this alkaloid was recently recorded in the Australian species *Zanthoxylum brachyacanthum* F. Muell. (Cannon *et al.* 1953). The cyclitol, *d*-quercitol (named (+)-*proto*quercitol by Angyal and Macdonald 1952) was also isolated in small yield.

Experimental

Analyses are by Miss J. Fildes, University of Sydney.

(*a*) *Extraction.*—The dried milled root-bark (9 kg.) was exhausted with methanol in a continuous extractor and the extract concentrated to 1500 cc. After standing for several weeks in a refrigerator the brown liquid had deposited a mixture of crystals and amorphous material. By swirling with a little methanol the lighter amorphous material was separated from the heavier crystals, which were subsequently identified as *d*-quercitol (0·025% yield).

The mother liquors were concentrated as far as possible under reduced pressure and the black viscous residue extracted with several portions of hot 1% hydrochloric acid until alkaloid tests were negative. The extract was kept for 2 days in the refrigerator, then saturated with potassium iodide, filtered, and exhausted with chloroform. Evaporation of the chloroform left the crude alkaloid as colourless needles (0·1% yield).

(*b*) *Identification of* d-*Quercitol.*—Crystallization from 70% aqueous methanol gave colourless prisms, m.p. 234 °C., $[\alpha]_D^{20°}$ +22° (*c*, 1·14% in water) which gave an iodoform test (Found: C, 43·7; H, 7·7%. Calc. for $C_6H_{12}O_5$: C, 43·9; H, 7·4%). According to van der Haar (1922) *d*-quercitol gives an iodoform test and has m.p. 233–234 °C., $[\alpha]_D^{25°}$ +24°.

Benzoylation in pyridine with benzoyl chloride gave the pentabenzoyl derivative which was recrystallized from ethanol as colourless needles, m.p. 155 °C., $[\alpha]_D^{15°}$ +59·5° (*c*, 1·16% in chloroform). Bauer and Moll (1942) record m.p. 155 °C., $[\alpha]_D^{23°}$ +61·4°.

(*c*) *Identification of* iso*Corydine Methiodide.*—The crude alkaloid was recrystallized first from dilute aqueous potassium iodide and then from absolute ethanol giving colourless needles, m.p. 229 °C. (decomp.), $[\alpha]_D^{20°}$ +132° (*c*, 1·71% in water) (Found: C, 52·0; H, 5·4; N, 2·5; I, 26·5%. Calc. for $C_{21}H_{26}O_4NI$: C, 52·3; H, 5·5; N, 2·9; I, 26·2).

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The values recorded for *iso*corydine methiodide are m.p. 224–225 °C. (Barger and Sargent 1939) and $[\alpha]_D^{20°}+143·3°$ (*c*, 1·02% in 50% ethanol) (Gadamer 1911). The ultraviolet absorption spectrum and the X-ray powder photograph were respectively identical with those of an authentic specimen.

Methylation of the alkaloid by the method of Cannon *et al.* (loc. cit.) gave colourless needles, m.p. 258 °C. (decomp.), $[\alpha]_D^{24°}+180°$ (*c*, 0·48% in water). An authentic sample had m.p. 258 °C. (decomp.), $[\alpha]_D^{25°}+180°$ (*c*, 0·48% in water).

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